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ANNUAL REPORTS

OF THE

CHEMICAL LABORATORY

OF THE

AMERICAN MEDICAL ASSOCIATION

VOLUME 16. JAN.-DEC. 1923

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VOLUME 16

JANUARY-DECEMBER, 1923

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PART I.	REPRINT OF CONTRIBUTIONS
PART II. . . .	REPORTS EXTRACTED FROM THE JOURNAL AND FROM HYGEIA
PART III.	REPORTS NOT PREVIOUSLY PUBLISHED

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PREFACE

The Chemical Laboratory of the American Medical Association was established in 1906 to assist the Council on Pharmacy and Chemistry of the American Medical Association in the investigation of proprietary and unofficial non-proprietary medicinal preparations offered to the medical profession.

In accordance with the object of its foundation, the A. M. A. Chemical Laboratory concerns itself primarily with the examination of those proprietary and unofficial medicinal preparations which the Council has under consideration. The Laboratory determines whether the claims made for the composition of these preparations are truthful, and, when a product is admitted to the Council's publication "New and Nonofficial Remedies," looks after the establishment of standards whereby the identity and purity of such a product may be determined.

In addition to the investigations made for the Council on Pharmacy and Chemistry, the Laboratory aids The Journal of the American Medical Association in supplying the medical profession and the public with information about the character and composition of drugs. This includes the analyses of proprietary medicinal preparations which are offered to the medical profession and which are not deemed worthy of investigation by the Council on Pharmacy and Chemistry, and the analyses of nostrums ("patent medicines") exploited to the public. Through the columns of The Journal and through direct correspondence the Laboratory responds to requests of physicians for information regarding proprietary preparations advertised to physicians and quack nostrums sold to the public, which have come to their notice. A knowledge of the composition of nostrums, whether offered to the medical profession or to the lay public, is generally a sufficient demonstration that many of the therapeutic claims made for such preparations are unwarranted. For this reason the Laboratory strives earnestly to answer all such inquiries, either by reference to available information or by actual analysis, when it is believed that the results of such investigation will prove of general interest to the medical profession or to the public.

This volume of the Reports of the A. M. A. Chemical Laboratory contains those portions of the Laboratory's activities during 1923 which were believed to be of interest to workers concerned with the examination and standardization of medicines, and includes: (1) reprints of contributions from the Chemical Laboratory of the American Medical Association, (2) reports abstracted from The Journal of the Americal Medical Association and from Hygeia and (3) reports not previously published. Continuing the practice adopted at the foundation of the Laboratory, each report in this volume contains a detailed statement of the analytical methods employed and the results obtained, whenever it was believed that such statement would prove helpful to others engaged in the examination of medicines.

CONTENTS

PAGE
Preface 3
Incompatibility of Mercurochrome-220 Soluble with Local Anesthetics and Alkaloids by L. E. Warren, Ph.C., B.S. 7
Identification of Some Local Anesthetics by L. E. Warren, Ph.C., B.S 10
Examination of American-made Chloramine-T, Dichloramine-T, Halazone and Preparations by Paul Nicholas Leech, Ph.D 27
The Chemical Examination of Some Commercial Brands of Carbon Tetrachlorid by L. E. Warren, Ph.C., B.S. 42
Quayle's "Bob-White Habit Sinkers" 52
Allen's Goiter Treatment 55
Peralga 58
Owl Enamel Toilet Cream 62
El Zair 65
Van Ess 70
Money in Mud 74
Slendaform 84
Gly-So-Iodonate 87
Note on a Compound of Benzocain with Iodin by L. E. Warren, Ph.C., B.S 97
Eskosan and Eskosan Cum Methyl Salicylate 99
Note on Frontier Asthma Co. Treatment 100
Neo-Silvol 101

PART I

REPRINTS OF CONTRIBUTIONS FROM THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION

INCOMPATIBILITY OF MERCUROCHROME-220 SOLUBLE WITH LOCAL ANESTHETICS AND ALKALOIDS

(Reprinted, with additions, from The Journal A. M. A., April 14, 1923, p. 1091)

L. E. Warren, Ph.C., B.S.

In The Journal, April 7, 1923, p. 1023, a letter was published from Dr. Charles E. Stolz, entitled "Caution in Use of Mercurochrome-220 Soluble" in which he reported an accident in treatment owing to an apparent precipitation of the drug by procain. Fortunately the results were not serious, but, in view of our rather meager knowledge of the chemical properties of mercurochrome-220 soluble, it seemed desirable to study its incompatibilities further with the view of preventing future mishaps. Accordingly experiments were undertaken with the view of verifying Dr. Stolz' observation with procain and also to determine whether other local anesthetics than procain were incompatible with mercurochrome-220 soluble. It is well known that many basic substances, such as alkaloids and local anesthetics, are precipitated by certain complex mercury salts; but Dr. Stolz appears to have been the first to observe an incompatibility between mercurochrome-220 soluble and a local anesthetic.

Chemically mercurochrome-220 soluble is the disodium salt of dibromo-oxymercuri-fluorescein. If treated with an acid the sodium combines with the acid radical and the bromomercuri-fluorescein complex is precipitated as an insoluble compound having acidic properties.

In these tests a small portion of a 2 per cent. aqueous solution of each of several local anesthetics was treated with a few drops of a 2 per cent. aqueous solution of mercurochrome-220 soluble. The strength of 2 per cent. for each substance was selected because this was assumed to represent a fair average of the concentration in which the several substances are employed in medicine. In cases of scant solubility of the anesthetic substance in water a few drops of diluted hydrochloric acid were added in order to render the material soluble.

The following substances gave precipitates: alypin, apothesine, benzocain, butyn, cocain hydrochlorid, B-eucain lactate, phenacain, procain, propaesin, quinin and urea hydrochlorid, tropacocain hydrochlorid and stovain.

The precipitate in each case was of a deep red color, was amorphous and did not become crystalline on standing. In some instances analysis of the dried precipitate showed that it contained all of the essential constituents of the dibromo-oxymercuri-fluorescein radical viz., bromin, mercury and the dye substance, but that it did not contain sodium or the acid radical with which the basic substance was originally combined. Preliminary tests indicated that the precipitates were probably too soluble to be of value in the analytic separation of the local anesthetics from other substances but that they were sufficiently insoluble to render dangerous the concomitant prescribing of one of the local anesthetics and mercurochrome-220 soluble. The test was also applied to aqueous solutions of benzyl alcohol and saligenin, substances which have local anesthetic properties but which do not have basic properties. No precipitate was given with either substance .

As a matter of interest the test was applied to a salt of a number of vegetable alkaloids or their derivatives in aqueous solution. A red precipitate was given with each of the following substances: aconitin hydrochlorid, apomorphin hydrochlorid, atropin sulphate, brucin hydrochlorid, cephaelin hydrochlorid, cinchonidin sulphate, cinchonin sulphate, codein sulphate, diacetyl-morphin hydrochlorid, emetin hydrochlorid, ethyl hydrocuprein hydrochlorid, ethyl morphin hydrochlorid, gelsemin hydrochlorid, homatropin hydrochlorid, hydrastin hydrochlorid, morphin sulphate, narcein hydrochlorid, narcotin hydrochlorid, nicotin hydrochlorid, papaverin hydrochlorid, physostigmin sulphate, pilocarpin nitrate, quinidin sulphate, quinin hydrochlorid, sanguinarin hydrochlorid, scopolamin hydrobromid, solanin hydrochlorid, spartein sulphate, strychnin sulphate and thebain hydrochlorid.

As in the case of the local anesthetics the precipitates appeared to be too soluble for the reaction to be of much value in the analytic determinations of the alkaloids. A few basic substances did not give any precipitate with mercurochrome-220 soluble. These were caffein, colchicin hydrochlorid, coniin hydrochlorid, methyl atropin bromid, theobromin sodium salicylate and theophyllin sodium acetate.

Details of Analysis

Mercury.—A 2 per cent. solution of procain nitrate was precipitated by an excess of a 2 per cent. solution of mercurochrome-220 soluble, the precipitate collected on a filter, washed with water and dried in the air at 50 C. Procain nitrate was used instead of the chlorid in order that the bromin might be determined later without interference from any possible adhering chlorid. A weighed portion of the dark red precipitate was treated in a Kjeldahl flask with sulphuric acid, potassium permanganate and oxalic acid according to the method described in the reports of the Chemical Laboratory of the American Medical Association, Vol. 13, p. 71 (1921) for the determination of mercury in mercurochrome-220 soluble. From 0.1879 gm. of the precipitate, 0.0593 gm. of mercuric sulphid was obtained, equivalent to 27.37 per cent. of mercury.

Bromin.—A weighed portion of the precipitate was treated in an all-glass reflux apparatus with fuming nitric acid and some solid silver nitrate. After the mixture had lost all of its dye color, it was diluted with water. A considerable quantity of a pale yellow precipitate was given. This was collected in a weighed Gooch crucible, dried at 120 C. and weighed. The precipitate was considered to be silver bromid. From 0.4609 gm. of material 0.1641 gm. of silver bromid was obtained ,equivalent to 15.15 per cent. of bromin.

Dye Substance.—A small quantity of the red precipitate was treated with a large excess of water. The material dissolved to form a red, fluorescent solution. This (together with previous experimental evidence) was taken to indicate that the precipitate contained the brom-mercuri-fluorescein radical.

Sodium.—The practical absence of sodium in the precipitate was demonstrated by precipitating a weighed quantity of mercurochrome-200 soluble so far as possible with an excess of procain nitrate and heating the precipitate in a weighed platinum dish with an excess of sulphuric acid, using some nitric acid at the end to facilitate oxidation. Almost no residue remained. In another test 0.0025 gm. of sodium sulphate was obtained from 0.1870 gm. of the dried precipitate. This was taken to indicate that in the reaction between mercurochrome-220 soluble and procain nitrate the sodium does not become a part of the precipitate. Further evidence of this supposition was offered by the following test: The filtrate from the precipitate obtained in the preceding test was evaporated to small volume and heated in a weighed platinum dish with an excess of sulphuric acid, more sulphuric acid and some nitric acid being repeatedly added toward the end to facilitate burning of the dye substance. The filtrate from 0.5282 gm. of mercurochrome-220 soluble, equivalent to 0.031692 gm. of sodium gave 0.0995 gm. of sodium sulphate. This is equivalent to 0.0322 gm. of sodium, or about 101 per cent. of the sodium theoretically present. Since this sodium sulphate was obtained from the filtrate after precipitation it becomes evident that the sodium does not become a part of the precipitate in the reaction between mercurochrome-220 soluble and procain nitrate.

Acid Radical.—A weighed quantity of butyn (0.2180 gm. equivalent to 0.747522 gm. of barium sulphate) was precipitated with an excess of mercurochrome-220 soluble, the precipitate collected on a filter and the sulphate in the filtrate determined by the barium sulphate method in the usual way. The barium sulphate obtained from the filtrate weighed 0.694 gm., or about 93 per cent. of the theoretical quantity. It is evident from this that not much of the sulphate radical goes with the butyn-mercurochrome-precipitate.

From the results of the analysis it was concluded that the precipitate probably contains all of the mercury and bromin in combination with the fluorescein complex as originally present in mercurochrome-220 soluble, but that it does not contain sodium or the acid radical with which the anesthetic substance was in combination originally.

THE IDENTIFICATION OF SOME LOCAL ANESTHETICS

(Reprinted from the Journal of the American Pharmaceutical Association, June, 1923, p. 512)

L. E. Warren, Ph.C., B.S.

During the last quarter of a century many organic substances have come into use in medicine because they possess the power of causing temporary loss of sensation when applied to the mucous surfaces, or by injection into the tissues. These substances are known as local anesthetics. Some are alkaloids occurring in nature, such as cocain and tropacocain, but most of them are synthetic bases whose physical and chemical properties resemble those of the naturally occurring alkaloids. The longest known of the local anesthetics is cocain. Together with other bases this occurs in *Erythroxylon coca* and other species of *Erythroxylon*, shrubs, native to the Andean region of South America. Although cocain was isolated in 1860[1] it was not until 1885[2] that its local anesthetic properties were sufficiently recognized to be made of practical value. Its use soon became widespread and for some years it remained the only known local anesthetic in practical use. However, cocain was found to be distinctly poisonous, it produced undesirable side effects, such as mydriasis, cloudiness of the cornea and habit formation, and its salts were not stable in solution.

Tropacocain was first found in coca leaves from Java.[3] It was found to be less poisonous than cocain and to possess greater local anesthetic action,[4] without the objectionable mydriatic properties of cocain. Further, the solutions of its salts were also less prone to decompose. It may be made synthetically by benzoylating pseudo-tropin.

Organic chemists, after working out the constitution of cocain, attempted to build up a synthetic substitute for it which would be less toxic and perhaps cheaper. One of the first successful ones was α-eucain.[5] This was found to be less toxic than cocain, cheaper and its solutions were stable on being heated. It had the disadvantage of causing pain and irritation when injected. Because of this it was superseded by β-eucain, benzoyl-vinyl diacetone-alkamin hydrochlorid.[6] This was found to be less toxic than α-eucain. The salt of β-eucain which is most used is the lactate because of its greater solubility than the hydrochlorid.

After the advent of β-eucain a great number of substances having local anesthetic properties were worked out by organic chemists. Many of them were more faulty than cocain in their chemical and pharmacologic properties so that they never came into extensive use. Others were found to have some special advantages and their use became more or less general. Holocain (phenacain),[7] orthoform,[8] acoin,[9] nirvanin,[10] anesthesin (benzocain),[11] alypin,[12] novocain (procain),[13] cycloform,[14] propaesin,[15] subcutin[16] and stovain[17] came in quick succession. Apothesine[18] and butyn[19] were developed recently, while the anesthetic properties of saligenin[20] were only recently discovered although the substance had been known to plant chemists for many years.* Some of these have been widely used, each for some real or fancied advantage, and several have been dignified by admission into the pharmacopeias. Most of them have been described in New and Nonofficial Remedies at one time or another.

The synthetic local anesthetics resemble cocain more or less in their structural relationships and they are, therefore, subject to about the same incompatibilities. In general they are precipitated by the usual alkaloidal reagents; consequently their separation in admixture is difficult. Fortunately they are rarely found together in medicine so that the analyst is usually required only to identify or determine but one at a time.

So far as the writer knows no systematic attempt has been reported heretofore to apply practically all of the commonly used alkaloidal reagents to all of the local anesthetics in common use. In these studies this has been done and the results tabulated for comparison. By this method some reactions have been observed which appear not to have been previously reported.

The literature on the chemical identification of local anesthetics is quite considerable, but is widely scattered. On that account no attempt is made here to review it systematically. The most comprehensive paper on the subject with which the writer is familiar is that by Hankin.[21] He recorded his observations on a large number of tests, and Saporetti[22] and Gadamer[23] are two others who have added much to the literature concerning tests for the local anesthetics. So far as practicable the work of these investigators has been repeated by the writer. In these studies but little attention has been paid to acoin, cycloform, α-eucain, subcutin or nirvanin, substances which were not available because they are no longer used in medicine—at least not to any extent in this country.

Several of the local anesthetics are described in New and Nonofficial Remedies. Several more that were formerly described in this work have been omitted because they were no longer available on the American market. Most of the observations recorded in this paper were made while preparing or revising the descriptions and tests for the identity and purity of the several substances for New and Nonofficial Remedies.

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* Recently benzyl alcohol and saligenin have been introduced as local anesthetics. Because of their relations to the alcohols they do not give many of the reactions for alkaloids. Benzyl alcohol is not included in these studies and but few tests were made on saligenin.

The alkaloidal solutions used in this work unless otherwise stated were prepared by dissolving 1 gm. of the substance in 50 c.c. of water, i. e., they were approximately 2 per cent. in strength. Substances which were practically insoluble in water, such as benzocain, orthoform and propaesin, were made soluble by suspending 1 gm. in 50 c.c. of water and adding just sufficient hydrochloric acid with shaking to produce solution. Care was taken to avoid an excess of acid. The reagent solutions used, unless otherwise stated, were the test solutions described in the U. S. Pharmacopeia. The nonofficial test solutions were approximately 10 per cent. in strength.

The precipitation tests were made by adding a few drops of the reagent to about 1 c.c. of the alkaloidal solution with agitation. If no precipitate formed or if the precipitate at first formed had been dissolved, a few drops more of the reagent were added with further agitation. This was repeated until it became evident either that no precipitate would form, or that the one formed either was permanent or had been dissolved by an excess of the reagent. Since most alkaloidal precipitates are amorphous when first thrown down but may become crystalline on standing, about ten minutes were allowed after the precipitation had taken place before recording the observation to determine whether or not the precipitate would become crystalline. In a few cases crystallization did not invariably begin within ten minutes and a longer time was allowed. These exceptions are mentioned in the description of the test. The results obtained in over 400 tests are recorded in the tables.

By a comparison of the tabulated reactions it is possible to identify each of the substances studied. However, since there is such a large number of reactions to be compared a simplified scheme has been worked out to aid in the rapid identification of the substances in question. This consists first in applying the diazoreaction by means of which the anesthetics are divided into two groups—i. e., (1) those which respond to the reaction and (2) those which do not. The diazo group (A) includes benzocain, butyn, orthoform, phenacain, procain and propaesin. The other group (B) includes alypin, apothesine, β-eucain, cocain, quinin and urea hydrochlorid, stovain and tropacocain. The second step consists in testing the solutions with a list of seven reagents in succession. By tabulating the results obtained it is possible to identify any of the local anesthetics mentioned since no two give exactly parallel reactions. The findings for the entire series of tests are given in Table I, while Table II comprises the simplified scheme of identification. Some of the reactions require more explanation than can be given in the tables and these are given later in the form of comments. In addition to the precipitation test several special tests were applied. For the sake of uniformity and completeness the results are included in the table. These tests are given herewith:

Diazo Reaction.—To 5 c.c. of a 2 per cent. solution of the substance add 2 drops of diluted hydrochloric acid, 2 drops of 10 per cent. sodium nitrite solution and mix with a solution of 0.2 gm. of β-naphthol in 10 c.c. of 10 per cent. sodium hydroxid solution. Certain of the local anesthetics give a deep red solution or scarlet precipitate.

Mercurous Chlorid Test.—Mix intimately about 0.1 gm. of the substance with 0.1 gm. of mercurous chlorid and moisten the mixture with alcohol. With certain of the local anesthetics a darkening of the mixture takes place.

Sodium Hypochlorite Test.—To about 1 c.c. of the alkaloidal solution add a few drops of sodium hypochlorite solution. If a flesh-colored precipitate be given, add 2 c.c. of ether, shake the mixture and observe the color of the solvent. Several of the local anesthetics give precipitates more or less approaching to flesh-color and when shaken with ether the solvent is colored more or less approaching a burgundy red.

In addition to the results obtained by the experimental work considerable information concerning the physical properties of the local anesthetics was collected from the literature. As this kind of information is often of great value to the analyst it is included in the tables and comments. Specific credit cannot be given in each instance to the numerous workers whose results have been drawn upon for this collation.

Nearly all of the local anesthetics in solution give precipitates with potassium mercuric iodid solution, picric acid solution and phosphotungstic acid solution. These reagents, therefore, are of but little use in aiding in the differentiation between the several substances. Iodin is another reagent which gives precipitates with most of these substances. (The benzocain precipitate with iodin solution is distinctive and this compound will be described later.) Certain other reagent solutions precipitate only a few of the substances; i. e., tannic acid test solution precipitates only alypin and butyn; potassium sulphocyanate solution only butyn and phenacain; potassium sodium tartrate only benzocain, propaesin and quinin and urea hydrochlorid.

Potassium permanganate solution is of considerable value in differentiating between the several substances. Apothesine, benzocain, butyn, phenacain, orthoform, and quinin and urea hydrochlorid are reduced at once. Alypin, β-eucain, cocain, stovain, and tropacocain retain their color for some time. Cocain precipitates with potassium permanganate, if the solution be not too dilute, in the form of violet crystals which occur in microscopically characteristic rhomboidal plates, often with an indentation at one corner. Alypin forms violet-red crystals but they are much less stable than the cocain compound. Tropacocain forms thick, short, violet-red prisms which are about as stable as the cocain permanganate but which cannot be mistaken microscopically for that compound. The precipitates with β-eucain and stovain are amorphous.

Recently potassium citrate solution was suggested as an alkaloidal reagent by Toplis.[24] This has been applied to the local anesthetics and has proved useful. Benzocain, butyn, orthoform, phenacain, propaesin, quinin and urea hydrochlorid and stovain are precipitated. Some of the precipitates are crystalline as may be seen by consulting Table I. Potassium iodid solution precipitates alypin, butyn, phenacain, and tropacocain. The character of the several precipitates is of importance and is described under the comments on the individual substances. Potassium sodium tartrate produces white, crystalline precipitates with benzocain, propaesin and quinin and urea hydrochlorid.

The synthetic local anesthetics differ from cocain and quinin and urea hydrochlorid in being optically inactive. So far as the writer has been able to ascertain from the literature this rule holds good. All of the substances tested in these studies except the two mentioned were optically inactive. Since cocain has pronounced optical properties it might be expected that tropacocain might also be optically active, but such is not the case.

Alypin.—Alypin is benzoxy-2-dimethylamino-methyl-1-dimethylaminobutane. It is a white, crystalline powder; odorless; taste bitter; hygroscopic. Alypin is soluble in water, alcohol and chloroform; insoluble in ether. It melts at 169° C. Alypin gives a cream-white precipitate with tannic acid solution, but the precipitate is soluble in excess of the reagent. Of the other substances tested only butyn behaved in a similar way. Alypin is distinguished from butyn by its failure to give the diazo-reaction. Alypin gives a white precipitate with potassium iodid. Butyn, phenacain and tropacocain react similarly. Alypin is distinguished from phenacain and tropacocain, however, by its failure to precipitate with sodium nitroprussid solution. It differs from benzocain, butyn, orthoform, phenacain, propaesin, quinin and urea hydrochlorid and stovain in not giving a precipitate with potassium citrate. Alypin gives a violet, crystalline precipitate with potassium permanganate solution but the precipitate is not so stable as that with cocain or tropacocain.

TABLE 1.—*Reactions of*

Reagent	Alypin	Benzocain (Anesthesin)	Apothesine	B-Eucain Lactate	Butyn	Cocain Hydrochlorid
Iodin and potassium iodid	Brown	Brown iridescent crystals	Red-brown	Brown precipitate; soluble on boiling	Drab	Brown
Potassium mercuric iodid	White; curdy	....	White	White	White	White
Potassium iodid	White; cryst.	....	....	....	White;	....
Mercuric chlorid	White; amorphous	Beautiful colorless needles on standing	White; amorphous	....	White; amorphous	White; cryst.
Phosphotungstic acid	White	White	White	White	White	White
Picric acid	Yellow masses; minute prisms	Yellow	Yellow; cryst.	Yellow; cryst.	Yellow; cryst.	Yellow; long needles
Sodium carbonate	White	White; cryst.	White	White	White	White
Sodium bicarbonate	....	White; soluble in excess	White; soluble in excess	....	White	White; colorless; slender needles
Gold chlorid	Pale lemon-yellow; cryst.	Brown	Lemon yellow	Lemon-yellow	Brown	Pale lemon-yellow; like fern fronds
Platinum chlorid HCl	Salmon; aggregate of minute prisms	Pale yellow; cryst.	Yellow; cryst.	Crystalline needles	Pale orange; amorphous	Yellow plumose needles
Palladium chlorid	Salmon	Yellowish white; gelatinous	Salmon	....	Yellowish brown	....
Chromic acid	....	....	Orange	Yellow large crystals	Orange-yellow cryst.	Add HCl; orange; cryst.
Bromin water	Yellow; soluble in hot water reappears on cooling	White; partly soluble in hot water	Yellow; soluble in hot water	Pale yellow; soluble on heating	White	Yellow; soluble on heating
Potassium cadmium iodid	White	....	White	White	White	White
Potassium zinc iodid	....	....	Pale yellow; beautiful needles	....	White	Pale yellow
Sodium salicylate	....	White	White; amorphous	White; cryst.	White	....
Sodium nitroprussid	....	....	Pale salmon; amorphous	....	Yellowish white; resin-like	....
Fehling's solution	White	White; cryst.	White	White	White	White; large prisms

Some Local Anesthetics

Phenacain (Holocain Hydrochlorid)	Orthoform	Procain	Quinin and Urea Hydrochlorid	Stovain	Tropacocain-Hydrochlorid	Propaesin
Brown	Brown: slow to form; then reduction	Brown	Brown	Brown	Brown	Brown
White; curdy	....	White	White	White to cream	White	White
White	....	....	....	....	White glistening scales	....
White	....	White: soluble in hot water	White; cryst.	White; soluble in excess	White; bulky; cryst.	....
White	White	White	White	White	White	White
Yellow; cryst.	Yellow; cryst.	Yellowish masses of needle-like prisms	Yellow	Yellow; cryst.	Yellow; minute needles	Yellow
White	....	White	White	White	White; amorphous	White
White	White; cryst.	....	White	White	....	White
Canary-yellow	Dirty, dark green	Brown	Orange-yellow	Yellow; cryst.	Yellow; pinnate prisms	Yellowish brown
Drab	....	Yellow	Pale yellow	....	Pale salmon; cryst.	Yellow; cryst.
Salmon	Pale yellow; cryst.	Brownish orange	Salmon	....	Salmon; fern-like cryst.	Salmon, flocculent
Orange-yellow	Blackens instantly	....	Orange	....	Yellow; fern-like	....
Yellowish brown; soluble on heating	Yellowish green; orange on boiling	Yellow; soluble in hot water	Yellow; soluble in hot water	Orange	Yellow; soluble on heating	White
White	....	Drab	Cream	White	White; cryst.; very bulky	....
Yellowish white	....	....	....	Yellow cloud	White; cryst.; bulky	....
White	....	....	Cream-white	....	....	White; cryst
Pale salmon; cryst.	....	....	....	....	Colorless; cryst.	....
White	Green; soluble in excess	White	White; curdy	White	White	White; cryst.

TABLE 1.—*Reactions of Some*

Reagent	Alypin	Benzocain (Anesthesin)	Apothesine	B-Eucain Lactate	Butyn	Cocain Hydrochlorid
Potassium sodium tartrate	....	White; cryst	....	....	....	....
Sodium Hypochlorite	White	Flesh-colored precipitate	Cream-white; curdy	White	Flesh-colored cryst.	White; amorphous
Potassium dichromate	Orange; cryst..	Darkens on standing	Yellow precipitate	Orange	Orange-yellow	Orange-red
Potassium permanganate	Violet; cryst. soon decomposes	Decomposes instantly	Decolorizes at once	Does not decompose at once	Decomposes instantly	Violet minute cryst.
Tannic acid	Cream-white; soluble in excess	....	....	....	Cream-white; curdy; soluble in excess	....
Potassium citrate	....	White; cryst.	....	....	White; amorphous	....
Potassium chromate	Yellow; cryst.; slow to form	Orange; cryst.	Greenish yellow cloud	....	Orange-yellow; cryst.; reduces on standing	Add HCl; orange precipitate
Potassium bismuth iodid	White	Orange; cryst.	Orange	....	White cryst.	....
Sodium borate	White	White; cryst.	White	....	White	....
Potassium ferricyanid	....	....	Lemon-yellow; oily	....	Brownish yellow oil	....
Mercurous chlorid	Darkens	No change	Darkens	No change	No change	Blackens
Diazo-	White precipitate dissolves on standing	Dark ruby-red color	White precipitate dissolves on standing	White precipitate soon dissolves	Red	White precipitate soon dissolves
Potassium sulphocyanate	....	....	... .	....	White; amorphous	....

Apothesine.—Apothesine is the hydrochlorid of diethyl-amino-propyl cinnamate. It occurs in white, odorless masses which are composed of minute, colorless needles. It is soluble in water, alcohol and chloroform; insoluble in ether. Its taste is slightly bitter. It gives precipitates with potassium mercuric iodid solution, bromin water (soluble in hot water), sodium bicarbonate (soluble in excess), sodium borate, sodium salicylate, sodium nitroprussid, gold chlorid (lemon-yellow), platinum chlorid (yellow crystals) and palladium chlorid (salmon). It is distinguished from other local anesthetics tested by the character of its precipitate with

Local Anesthetics—(Continued)

Phenacain (Holocain Hydrochlorid)	Orthoform	Procain	Quinin and Urea Hydrochlorid	Stovain	Tropacocain-Hydrochlorid	Propaesin
....	....	....	White; cryst.	....	....	White; cryst.
Flesh-colored becoming violet	Grayish brown	Flesh-colored	Cream-white; curdy; becoming cryst.	White; amorphous	White; cryst.	Flesh-colored
Yellow	Black; reduces instantly	....	Orange	....	Orange-red; cryst.	....
Reduces at once	Reduces at once	Decomposes immediately	Reduces instantly	Reduces slowly	Violet; cryst.	Reduces instantly
....	....	....	....	....	....	....
White; amorphous	White; cryst.	....	White; cryst.	White; amorphous	....	White; cryst.
Yellow	Black; reduces instantly	....	Yellow; cryst.	Yellow	....	Orange; cryst.
Orange	....	....	Orange	....	Bulky white; cryst.	Orange
White	....	....	White	White	White; amorphous	White; cryst.
Brownish yellow	....	....	Pale yellow; soluble in excess	....	Needle-like; cryst.	....
No change	No change	Blackens	Darkens	Darkens	Darkens	No change
Scarlet	Dark red color	Scarlet precipitate	White; dissolves on standing	No color	Yellow	Scarlet
White rosettes	....	....	....	....	....	....

sodium nitroprussid. Of the others tested only butyn, phenacain and tropacocain give precipitates with this reagent. Of these butyn alone gives an amorphous precipitate which is yellowish-white in color and of a resin-like consistency. The apothesine precipitate is not resin-like and is of a salmon color. Butyn base and apothesine base are liquid; phenacain base melts at 116-7° C., while tropacocain base melts at 49° C. A color reaction for apothesine which appears to be characteristic is that with Marquis' reagent. About 0.01 gm. of apothesine is treated with a few drops of sulphuric acid containing a trace of formaldehyde.

The mixture is colorless at first but soon a pale brownish rose color develops which gradually changes to an intense mahogany brown. The isolated base responds to the test fully as well as the hydrochlorid. It is believed that this reaction has not been described previously.

Benzocain.—Benzocain is ethyl amino-benzoate. It is a white, crystalline, odorless powder almost insoluble in water but soluble in very dilute hydrochloric acid. The most characteristic tests for benzocain are with iodin test solution and mercuric chlorid solution. With iodin solution benzocain produces beautiful, iridescent crystals. The precipitate is slow to form and is aided by gentle shaking of the test-tube. In absence of confirmatory tests the precipitate might be mistaken for herapathite. With mercuric chlorid test solution benzocain forms beautiful, colorless needles on standing. This reaction takes place slowly and is best observed after the mixed solutions have stood for 30 minutes. Of the other substances tested several (cocain, quinin and urea hydrochlorid and tropacocain) gave white, crystalline precipitates with mercuric chlorid but none gave such long, slender needles as were obtained with benzocain. It is believed that this reaction has not been described previously. Benzocain gives the diazo-reaction but this does not distinguish it from butyn, orthoform, procain or propaesin, each of which responds to the test. However, two of these substances may be distinguished from benzocain by the physical properties of their separated bases. Butyn base is liquid at ordinary temperatures and procain base melts at about 58 to 60 C. The melting point of benzocain is 90 to 91 C., and that of propaesin 73 C. Propaesin is not precipitated by mercuric chlorid. Orthoform is not precipitated by potassium sodium tartrate (as is benzocain). Quinin and urea hydrochlorid is precipitated by potassium sodium tartrate (as well as benzocain) but this substance is readily distinguished from benzocain by its failure to give the diazo-reaction and by its strong fluorescence with very dilute sulphuric acid. Benzocain does not darken with mercurous chlorid and alcohol (difference from alypin, apothesine, cocain, procain, quinin and urea hydrochlorid, stovain and tropacocain).

Cocain Hydrochlorid.—Cocain hydrochlorid, methyl benzoyl ecgonin hydrochlorid, is official in the U. S. Pharmacopœia. It occurs in white, crystalline masses; odorless; permanent in the air. It is soluble in water, alcohol and chloroform; insoluble in ether. Cocain hydrochlorid is precipitated by mercuric chlorid, sodium carbonate, sodium bicarbonate, potassium permanganate and Fehling's solution. It is darkened by mercurous chlorid and alcohol (*difference from β-eucain*). Its precipitate with potassium permanganate occurs in violet, rhomboidal plates which frequently have an indentation at one corner and which are more stable than the permanganates of the other local anesthetics. It is distinguished from alypin by its failure to precipitate with potassium iodid, tannic acid solution or sodium borate; from benzocain by its failure to precipitate with potassium bismuth iodid or potassium sodium tartrate or to give the diazo-reaction; and by its precipitation with potassium cadmium iodid and by its positive reaction with mercurous chlorid and alcohol; from β-eucain by its precipitation with sodium bicarbonate and mercuric chlorid and by its positive reaction with mercurous chlorid and alcohol; from apothesine by its failure to precipitate with sodium salicylate, sodium nitroprussid, sodium borate or potassium ferricyanid; from phenacain by its failure to precipitate with potassium iodid, sodium nitroprussid, potassium citrate, sodium borate or potassium sulphocyanate; from butyn by its failure to precipitate with potassium iodid, sodium salicylate, sodium nitroprussid, tannic acid, potassium citrate, sodium borate or potassium sulphocyanate; from orthoform by its precipitation with potassium mercuric iodid, picric acid, sodium carbonate and potassium cadmium iodid and by its failure to precipitate with potassium citrate or to give the diazo-reaction. Further, it does not reduce chromic acid, potassium permanganate or gold chlorid as does orthoform. Cocain is distinguished from procain by its precipitation with sodium bicarbonate or chromic acid (after adding hydrochloric acid), by its failure to give the diazoreaction or to reduce potassium permanganate immediately; from quinin and urea hydrochlorid by its failure to precipitate with sodium salicylate, potassium citrate, potassium ferricyanid or sodium borate; from propaesin by its precipitation with mercuric chlorid, chromic acid (after adding hydrochloric acid), potassium cadmium iodid or sodium borate and by its failure to precipitate with potassium tartrate, potassium citrate or sodium borate; from stovain by its precipitation with chromic acid (after the addition of hydrochloric acid) and by its failure to precipitate with potassium citrate or sodium borate; and from tropacocain by its failure to precipitate with potassium iodid, sodium nitroprussid, potassium bismuth iodid, sodium borate or potassium ferricyanide, and by its precipitation with sodium bicarbonate.

β-Eucain Lactate.—β-Eucain is trimethyl-benzoyl-oxy-piperidin. It is official in the U. S. Pharmacopœia in the form of its chlorid. β-Eucain lactate is a white, crystalline powder; odorless; permanent in the air. It is soluble in water, alcohol and chloroform, but only slightly soluble in ether. β-Eucain lactate is precipitated by sodium salicylate, bromin water, chromic acid, gold chlorid and Fehling's solution. It is distinguished from cocain by its failure to precipitate with mercuric chlorid and sodium bicarbonate, by its precipitation with sodium salicylate, by its optical inactivity, and by the fact that it does not darken with the mercurous chlorid and alcohol test; from phenacain by its failure to precipitate with mercuric chlorid, sodium bicarbonate, sodium nitroprussid, potassium iodid, potassium citrate, sodium borate, and potassium ferricyanid; from procain by its failure to precipitate with mercuric chlorid or to give the diazo-reaction and by its precipitation with chromic acid and sodum salicylate. β-Eucain is distinguished from stovain by its precipitation with chromic acid, sodium salicylate and potassium dichromate and by its failure to precipitate with mercuric chlorid, sodium bicarbonate or potassium citrate; from tropacocain by its failure to precipitate with potassium iodid, mercuric chlorid, sodium nitroprussid, sodium borate or potassium ferricyanid.

Butyn.—This is *p*-aminobenzoyl-γ-dinormalbutylaminopropanol sulphate. It is a white, hygroscopic solid; very soluble in water; soluble in alcohol and chloroform; insoluble in ether. Butyn gives a white, curdy precipitate with potassium iodid solution. Of the other substances tested alypin, phenacain and tropacocain only give precipitates with this reagent. The alypin precipitate is crystalline, the tropacocain precipitate is in the form of glistening white scales and the phenacain precipitate does not form curds. Consequently this test is, in a sense, distinctive for butyn. Attempts to determine butyn by collecting the butyn-iodid compound and weighing it were not satisfactory. This is due to the fact that the precipitate is appreciably soluble in water. Butyn gives white, amorphous precipitates with potassium sulphocyanate, potassium citrate and mercuric chlorid solutions. It gives crystalline precipitates with chromic acid, potassium zinc iodid, sodium hypochlorite and potassium dichromate solutions. Since butyn is a sulphate it gives a precipitate with barium chlorid solution thus differing from other local anesthetics in common use. Butyn is distinguished from alypin by its precipitation with sodium bicarbonate, from apothesine by its precipitation with potassium iodid, potassium citrate, sodium borate, potassium ferricyanid, and potassium sulphocyanate; from cocain by its precipitation with sodium nitroprussid, potassium citrate and sodium borate; from phenacain by its precipitation with tannic acid; from orthoform by its precipitation with potassium iodid, picric acid and mercuric chlorid; from procain by its precipitation with potassium iodid, sodium bicarbonate and sodium nitroprussid, and from stovain by its precipitation with potassium iodid and sodium salicylate.

Orthoform.—Orthoform is *m*-amino-*p*-hydroxy benzoate. It is a white, odorless powder; almost insoluble in water, but soluble in dilute hydrochloric acid. Its insolubility in water distinguishes it from the other local anesthetics tested except benzocain and propaesin. It is soluble in ether, thus differing from most of the other local anesthetics, except benzocain and propaesin. No precipitate is given with picric acid. This distinguishes it from most other local anesthetics except saligenin. It is not precipitated by potassium mercuric iodid. It reduces chromic acid instantly; also potassium chromate and potassium dichromate, thus differing from all of the other substances tested. It gives a white, crystalline precipitate with potassium citrate. It gives the diazo-reaction, forming an intensely dark red solution. Orthoform (solid) gives an intensely black color with nitric acid which gradually changes to a rich, mahogany brown. Under the same conditions saligenin gives a yellowish brown color and phenacain slowly becomes brown, but none other of the substances tested gave reactions at all simulating the reaction with orthoform. Orthoform reduces potassium permanganate instantly, but it does not darken with mercurous chlorid and alcohol.

Phenacain.—Phenacain is ethenyl-*p*-diethoxy-diphenyl amidin hydrochlorid. It is soluble in about 50 parts of water; soluble in alcohol and chloroform; insoluble in ether. Phenacain is precipitated by potassium sulphocyanate in the form of white rosettes, a reaction which is distinctive and which appears not to have been noted previously. It also gives precipitates with potassium iodid, sodium nitroprussid, potassium citrate and mercuric chlorid. Phenacain is distinguished from benzocain, quinin and urea hydrochlorid and propaesin by its failure to precipitate with potassium sodium tartrate. With potassium sulphocyanate it gives white rosettes. Phenacain is precipitated by a larger number of reagents than is any other of the synthetic anesthetics tested.

Procain.—Procain is *p*-amino-benzoyldiethylamino-ethanol hydrochlorid. It is a white, odorless, crystalline powder; soluble in water, alcohol and chloroform; insoluble in ether. Procain gives the diazo-reaction and a white precipitate with mercuric chlorid soluton which is soluble in hot water. It is not precipitated by potassium citrate solution which distinguishes it from the other alkaloids of the diazo-group. It is not precipitated by sodium bicarbonate, chromic acid, sodium salicylate or potassium dichromate. It gives a brown precipitate with gold chlorid solution. It reduces potassium permanganate instantly.

Propaesin.—Propaesin is propyl-amino-benzoate. It occurs as a fine, white, odorless powder; permanent in the air. It is soluble in alcohol, ether and chloroform, but only slightly soluble in water. It is distinguished from alypin, butyn, phenacain and tropacocain by its failure to precipitate with potassium iodid; from benzocain and quinin and urea hydrochlorid by its failure to precipitate with mercuric chlorid; from apothesine and butyn by its failure to precipitate with chromic acid; from β-eucain by its failure to precipitate with sodium salicylate; and from cocain by its failure to precipitate with potassium cadmium iodid.

TABLE II.—*Reactions for the Rapid Identification of Local Anesthetics*

	Synthetic	Potassium Sulphocyanate	Potassium Iodin	Sodium Nitroprussid	Potassium Sodium Tartrate	Potassium Citrate	Potassium Permanganate	Mercuric Chlorid
A Diazo Group	Benzocain	...	...	...	White; cryst.	White; cryst.	Decomposes instantly	Beautiful, colorless needles (forms slowly)
	Butyn	White; amorphous	White	Yellowish white; resin-like	...	White; amorphous	Decomposes instantly	White; amorphous
	Orthoform	...	...	...	...	White; cryst.	Reduces instantly	...
	Phenacain	White; rosettes	White	Pale salmon; cryst.	...	White; amorphous	Reduces instantly	White
	Procain	...	...	...	...	...	Decomposes instantly	White; soluble in hot water
	Propaesin	...	...	...	White; cryst.	White; cryst.	Decomposes instantly	...
B Nondiazo-Group	Alypin	...	White; cryst.	...	...	...	Violet; cryst. not very stable	White; amorphous
	Apothesine	...	...	Pale salmon	...	...	Decomposes instantly	White; amorphous
	B-Eucain	...	...	...	...	...	Not decomposed at once	White; amorphous
	Cocain	...	...	...	...	...	Violet; cryst. quite stable	White; cryst.
	Quinin and urea hydrochlorid	...	...	...	White; cryst.	White; cryst.	Decomposes instantly	White; cryst.
	Stovain	...	...	...	...	White; amorphous	Decomposes slowly	White; soluble in excess
	Tropacocain	...	White; glistening scales	Colorless; cryst.	...	...	Violet; thick prisms	White; bulky; cryst.

Quinin and Urea Hydrochlorid.—Quinin possesses distinct local anesthetic properties, but many of its salts are too scantily soluble to be of good service in this field. By mixture with urea hydrochlorid the quinin salts become much more soluble. A mixture of equimolecular proportions of quinin hydrochlorid and urea hydrochlorid is very soluble in water and, before the advent of so many synthetic local anesthetics, this preparation had some vogue as a local anesthetic. Quinin and urea hydrochlorid occurs as a white, granular powder or in colorless, translucent prisms; odorless; taste bitter; soluble in water, alcohol and chloroform; insoluble in ether. Quinin and urea hydrochlorid precipitates with potassium ferricyanid but not with sodium nitroprussid,. thus distinguishing this substance from apothesine, butyn and phenacain which give precipitates with both reagents. Quinin and urea hydrochlorid is distinguished from all of the other substances tested by its strong fluorescence when dissolved in very dilute sulphuric acid. It is optically active, the specific rotation being about — 173.7° in water at 21 C. It is distinguished from alypin by its failure to precipitate with potassium iodid or tannic acid; from apothesine by its failure to precipitate with sodium nitroprussid; from benzocain by its precipitation with potassium ferricyanid and potassium mercuric iodid; from β-eucain by its precipitation with potassium sodium tartrate, potassium citrate, sodium bicarbonate and sodium borate; from cocain by its precipitation with potassium sodium tartrate, potassium citrate and sodium borate; from phenacain by its failure to precipitate with potassium iodid and potassium sulphocyanate; from procain by its precipitation with sodium bicarbonate, potassium sodium tartrate and potassium citrate; from propaesin by its precipitation with mercuric chlorid; from orthoform by its precipitation with picric acid; from stovain by its precipitation with palladium chlorid and potassium ferricyanid, and from tropacocain by its failure to precipitate with potassium iodid and sodium nitroprussid.

Saligenin.—Saligenin is *o*-hydroxy-benzyl alcohol. It is not precipitated by any of the ordinary alkaloidal precipitants except bromin water. With this reagent it forms pale yellowish white crystals. Since saligenin is a phenolmethylol it is probable that it might be estimated by adding an excess of bromin solution and titrating the excess as is done with phenols. It slowly reduces gold chlorid and instantly reduces potassium permanganate. It is optically inactive. Saligenin (solid) is instantly colored rose-red by concentrated sulphuric acid. None of the other local anesthetics tested gave this reaction. Saligenin (solid) with ferric chlorid solution gives a grass-green color which is persistent.

Stovain.—Stovain is ethyl-dimethylamino-benzoyl-pentanol hydrochlorid. Stovain occurs as a white, crystalline, odorless powder; soluble in water, alcohol and chloroform, but insoluble in ether. Stovain is precipitated by mercuric chlorid (soluble in excess), Fehling's solution, potassium citrate and sodium borate. It is not precipitated by sodium salicylate, sodium nitroprussid or potassium sodium tartrate. Stovain is distinguished from alypin, butyn, phenacain and tropacocain by its failure to precipitate with potassium iodid; from benzocain by its failure to precipitate with palladium chlorid; from apothesine and β-eucain by its failure to precipitate with sodium salicylate; and from cocain and quinin and urea hydrochlorid by its failure to precipitate with platinum chlorid. It is distinguished from orthoform by its precipitation with potassium mercuric iodid; from procain by its precipitation with sodium bicarbonate, and from propaesin by its precipitation with mercuric chlorid.

Tropacocain.—Tropacocain hydrochlorid is distinguished from cocain hydrochlorid in being optically inactive and in giving crystalline pre-

Table III.—*Physical Properties of the Local Anesthetics*

Anesthetic	Solubility in Water	Solubility in Alcohol	Solubility in Chloroform	Solubility in Ether	Melting Point	Melting Point of Base
Alypin	Soluble	Soluble	Soluble	Insoluble	169 C.	Liquid
Apothesine	Soluble	Soluble	Soluble	Insoluble	137 C.	Liquid at room temperature
Benzocain	Slightly soluble	Soluble	Soluble	Soluble	90–91 C.	90–91 C.
B-Eucain lactate	Soluble	Soluble	Soluble	Slightly soluble	152 C.	91 C.
Butyn	Soluble	Soluble	Slowly soluble	Insoluble	98–100 C.	Liquid
Cocain hydrochlorid	Soluble	Soluble	Soluble	Insoluble	183–191 C.	95–98 C.
Orthoform	Nearly insoluble	Soluble	Slightly soluble	Soluble	141–143 C.	....
Phenacain	Soluble	Soluble	Soluble	Insoluble	189 C.	116–117 C.
Procain	Soluble	Soluble	Soluble	Insoluble	153–155 C.	58–60 C.
Propaesin	Almost insoluble	Soluble	Soluble	Soluble	73 C.	....
Quinin and urea hydrochlorid	Soluble	Soluble	Soluble	Insoluble	....	....
Stovain	Soluble	Soluble	Soluble	Insoluble	175–176 C.	Liquid
Tropacocain hydrochlorid	Soluble	Soluble	Soluble	Insoluble	271–276 C. decomposes	49 C.

cipitates with potassium ferricyanid, sodium nitroprussid and potassium iodid. The last mentioned precipitate occurs in glistening white scales unlike the iodid of any other local anesthetic tested. The ferricyanid and nitroprussid tests also distinguish it from alypin, benzocain, orthoform, procain, propaesin, saligenin and stovain. Apothesine, butyn and phenacain give precipitates with both these reagents; butyn and phenacain give precipitates with potassium citrate and potassium sulphocyanate (which tropacocain does not do) and apothesine is not precipitated by potassium iodid as is tropacocain. Further, tropacocain differs from cocain in the crystalline form of its permanganate as has been noted under cocain.

SUMMARY

The usual alkaloidal reagents have been applied to 2 per cent. solutions of alypin, apothesine, benzocain, β-eucain, butyn, cocain hydrochlorid orthoform, phenacain, procain, propaesin, quinin and urea hydrochlorid, stovain, and tropacocain hydrochlorid. Observations on the optical activity of the substances studied were also made and a few color reactions were included. In a total of over 400 tests several reactions were observed which it is believed have not been reported previously. Several of these reactions are of particular value in the identification of the substances. A method for the rapid identification of certain local anesthetics has been worked out. This consists in first applying the diazo reaction by which the substances are separated into two groups. This is followed by treating separate portions of the unknown solution, respectively, with potassium sulphocyanate, potassium iodid, sodium nitroprussid, potassium sodium tartrate, potassium citrate, potassium permanganate and mercuric chlorid. In these tests no two of the substances studied give parallel reactions.

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SYNTHETIC DRUGS—IV

EXAMINATION OF AMERICAN-MADE CHLORAMINE-T, DICHLORAMINE-T, HALAZONE AND PREPARATIONS

(Reprinted from The Journal of the American Pharmaceutical Association, Vol. XII, No. 7, July, 1923, pp. 592-602)

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Six years ago Dakin, Cohen and Kenyon[1] introduced into medicine the first "chloramine" antiseptic, "Chloramine-T"; the other members of the family, "Dichloramin-T" and "Halazone,' 'followed soon afterward. The history of their introduction and of their commercial preparation has been detailed repeatedly in the pharmaceutical and medical literature; discussion now would be repetition.

The Council on Pharmacy and Chemistry of the American Medical Association kept pace with the therapeutic progress attendant on war times and described these chlorine antiseptics in New and Nonofficial Remedies after standards had been drawn up by the A. M. A. Chemical Laboratory. Since then a number of American firms have been marketing the products. It seemed opportune at this time to determine the purity of the market supply of those products described in New and Nonofficial Remedies and particularly to investigate the stability of the compounds containing a somwhat unstable atom. Hence this present report.

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[1] British Med. Jour., Jan. 29, 1916, p. 160.

The previous articles were: "Examination of American-Made Acetylsalicylic Acid," J. Ind. and Eng. Chem., April, 1918, p. 228 (see also editorial, ibid., April, 1918, p. 225); "American-Made Synthetic Drugs—II. Examination of Procaine (Novocain), Barbital (Veronal), Phenetidyl-acetphenetidin (Holocain), Cinchophen (Atophan), manufactured under Federal Trade Licenses" (with Wm. Rabak and A. H. Clark), J. A. M. A. **73:** 754 (Sept. 6) 1919; "Synthetic Drugs—III. The Digestion of Tannin Compounds Used as Intestinal Astringents by Artificial Digestive Mixtures," J. A. M. A. **75:** 1120 (Oct. 23) 1920.

COMPARISON OF CHLORAMINES AND "SURGICAL SOLUTION OF CHLORINATED SODA"

The chloramines and their predecessor "Surgical Solution of Chlorinated Soda" ("Dakin's Solution") have one point in common which seemingly has been overlooked in the many comments on this topic. Both possess the positively charged and relatively unstable chlorine atom (Cl^+) and hence are active oxidizing agents in the proper medium. Many writers have stressed the point that the Surgical Solution of Chlorinated Soda differs from the chloramines because it liberates oxygen and is, therefore, an oxidizing agent.[2] This explanation is a relic of past days when sodium hypochlorite or hypochlorous acid was presumed to act as $2HClO \rightarrow 2HCl + O_2$.

In the light of modern chemistry, however, we no longer hold the view that oxygen, directly or indirectly, is necessary for oxidation. Instead oxidation may "be considered to involve ultimately the assumption of positive or the loss of negative electrical charges by ions or atoms" and defined "as consisting fundamentally in the *loss of electrons by atoms or ions.*"[3] Thus hypochlorous acid [($ClOH$] which besides ionizing to H^+ and ClO^-, dissociates to Cl^+ and OH]; hypobromous acid Br^+OH^-) and their derivatives have a common characteristic, an atom with an unstable positive charge and a tendency to convert this atom to the common stable negative variety[4] (as for instance Chloride (Cl^-)).

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[2] The two main attributes of the Surgical Solution of Chlorinated Soda are: (1) a definite degree of alkalinity sufficient to be of value in removing necrotic tissue, but not too great to be unduly irritating; the *p*H should be between 8 and 10; (2) the solution should be hypertonic. For methods of preparing such a solution see "New and Nonofficial Remedies," 1922, p. 137.

[3] Julius Stieglitz: "Quantitative Chemical Analysis," The Century Company, 1911, Part I, p. 252.

There is convincing evidence to show that chloramine antiseptics contain positively charged chlorine: (1) The formulas and the methods of preparation (the replacing of a hydrogen atom of an amid group by chlorine) strongly suggest that the chlorine is positively charged. (2) On hydrolysis they yield hypochlorous acid. (3) They are active oxidizing agents.

Thus the chloramines may be considered as simply more adaptable forms of administering the positive chlorine, which is well known medically in the form of sodium hypochlorite (Cl^+ONa), or bleaching powder. The antiseptic action of these is most probably due to the oxidizing action of a positively charged chlorine, in the case of the hypochlorite, the chlorine atom is bound to a hydroxyl group; in the case of the chloramine, to a nitrogen ($N=$) atom.[5]

OXIDIZING ACTION OF CHLORAMINE-T

Accepting the premise that Chloramine-T is an antiseptic by oxidation because it contains the relatively unstable chlorine atom (Cl^+), which tends to go over to the stable form (Cl^-), the question arises what effect will the reaction of the solvent have on the oxidation potential. Is it more active in acid; neutral or alkaline solution? In elaborating Chloramine-T standards for the Council on Pharmacy and Chemistry, one of the first reactions noted was that when a dilute solution of Chloramine-T was added to potassium iodide solution, iodine was freed, but in the case of potassium bromide solution, no bromine was freed; yet, when the latter solution was acidified, bromine was freed. In fact, this test can be used advantageously for a simple qualitative distinction between bromides and iodides. This shows that the oxidating action is increased in acid solution, and that, in common with ferric chloride, Chloramine-T in neutral solution has sufficient oxidizing action to oxidize an iodide ion, but not sufficient to oxidize the relatively more stable bromide ion (Br^-). Some experiments were made by utilizing the electrometric measurement of the oxidation potential. When 1 gram of Chloramine-T[6] was added to 100 c.c. of a solution having a *p*H of 9, the voltage reading (using platinum electrode connected with the positive pole of the galvanometer[7]) was 0.12 V. When 1 gram of Chloramine-T was dissolved in 100 c.c. of water, having a p_H of 7 (the calomel[8] cell was connected to the positive pole of the galvanometer), the voltage reading was 0.4. When the solution was acidified, the voltage, of course, was increased enormously. Obviously this shows that Chloramine-T is greatly activated as an oxidizing agent when the medium is acid, whereas in alkaline solutions its oxidizing power is lowered proportionally to the concentration of the hydroxyl ions and it even acts as a reducing solution. As the bactericidal power of Chloramine-T is due probably to the oxidizing action (Cl^+), the question of the reaction of the medium is very important. The statement that Chloramine-T is fifty times more active as a germicide than phenol may be entirely wrong in certain media. There is great need for bacteriologic work to determine whether or not in an alkaline solution Chloramine-T has marked antiseptic value such as exists in an aromatic powder containing sodium bicarbonate. In fact, from these experiments, it would not be surprising to find that the hydrogen ion concentration (C_H), the oxidation potential and the bactericidal coefficient would be in direct ratio and that Chloramine-T is weakly antiseptic in alkaline solutions. It is hoped that some investigators will take up work along this line .

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[4] Stieglitz and Senior: J. Am. Chem. Soc. **38**: 2727, 1916.

[5] Those interested in the electronic aspect of the nitrogen valences are referred to Stieglitz and Leech, J. Am. Chem. Soc., Feb., 1914, 36, p. 272, and to references therein; also Stieglitz, ibid., June, 1922, 44, p. 1293.

PURITY OF MARKET SUPPLY OF CHLORAMINE-T AND PREPARATIONS

The essential standards of purity for Chloramine-T (sodium para-toluene sulphochloramid $CH_3C_6H_4SO_2NaN{-}Cl^+ + 3H_2O$, 1:4) are described in New and Nonofficial Remedies. The determinations reported in this paper are (1) loss in weight at 100–102° C., (2) decomposition (melting point), and (3) chlorine content (active chlorine).[9,10] The specimens were purchased on the open market in original containers. They were received during the latter part of November and the first of December, 1921, and kept in the dark until the analysis was made in June, 1922.

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[6] This sample of Chloramine-T contained no free alkali and its solution reacted neutral to phenolphthalein and to methyl red.

[7] The Wendt Electro-Titration Apparatus was used.

[8] Using normal potassium chloride solution.

[9] It is not uncommon to find chemists using the term "available" chlorine, irrespective of what factor is employed. In these determinations, the actual content of positively charged chlorine is determined, that is, the amount of the active form of chlorine. Available chlorine is calculated on the assumption that the positive chlorine (Cl^+) takes up an atom of negative chlorine (Cl^-) forming a molecule of chlorine, Cl_2 ($Cl^- — Cl^+$). This terminology probably is a hangover from the archaic of chlorides. It would seem that the time has come for the Pharmacopœia

Chloramine-T Powder.—All the recent specimens of Chloramine-T contain some free alkali. Of the specimens examined, one of the Squibb samples was considerably below the standard in both chlorine and water, while the other two Squibb samples and the Calco product did not contain the correct amount of moisture. The remaining products more

Table I.—*Chloramine-T Powder*

Brand	Loss in Weight at 100 C.	Melting Point	Chlorin (Cl^+) Content
Chloramine-T—Calco (Manufacturers).....	11.4	158	12.2 12.2
Chloramine-T—Monsanto (Baltimore)... .	17.8	163	12.50 12.50
Chloramine-T—Monsanto (Chicago)........	17.8	162	12.50 12.50
Chloramine-T—Squibb (Baltimore..........	13.4	169	12.2 12.2
Chloramine-T—Squibb (Chicago)...........	8.4	166	10.9 10.9
Chloramine-T—Squibb (New York).........	13.9	163	12.7 12.7
Chlorazene—Abbott (Baltimore)............	18.5	160	11.94 12.00
Chlorazene—Abbott (Chicago)..............	17.3	159	11.66 11.84
Chlorazene—Abbott (New York)............	17.6	159	12.48 12.47
"N. N. R."..................................	18-20	160-185	12-13

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method of determining the strength of hypochlorites by measuring the amount of chlorine evolved under appropriate treatment in the presence and books of reference to give analytical figures on the actual amount of the reactive substance and to discard the term "available." Whenever the figures for "available chlorine" are given, the mathematical value is just twice the actual amount of positively charged chlorine present (Cl^+).

10. The assay methods are as follows: If 1 gram of Chloramine-T is dried at from 100-102° C. for two hours, it loses not less than 18 per cent. nor more than 20 per cent. (water of hydration). If about 0.5 gram of Chloramine-T (accurately weighed) is dissolved in 50 c.c. of water, 10 c.c. of potassium iodid (10 per cent.) and 5 c.c. of acetic acid (36 per cent.) added and titrated with tenth-normal sodium thiosulphate, the chlorine content should not be higher than 13 per cent., or lower than 12 per cent. Each cubic centimeter of tenth-normal thiosulphate solution is equivalent to 0.00177 grams of chlorine.

closely approximate the "N. N. R." standards.[11] As may be seen from Table I, the products as found on the market are evidently quite stable.

Chloramine-T Tablets.—There are two brands described in "N. N. R.": Chloramine-T Tablets-Squibb and Chlorazene Tablets-Abbott; each is claimed to contain 4.6 grains of Chloramine-T. The tablets were weighed and then assayed, the results appearing in Table II. The tablets as found on the market are quite satisfactory.

TABLE II.—*Analysis of "Chloramine-T Tablets, 4.6 Grains"*

	Weight of Tablet		Amount of Chloramine-T Found	
Brand	Grams	Grains	Grams	Grains
Chloramine-T—Squibb (Baltimore)	0.2995	4.62	0.2911	4.49
	0.2951	4.55	0.2863	4.41
	0.3176	4.89	0.3060	4.72
	0.2901	4.47	0.2850	4.30
Chloramine-T—Squibb (New York)	0.2998	4.62	0.3006	4.63
	0.2937	4.53	0.2934	4.53
Chloramine-T—Squibb (Chicago)..	0.2935	4.53	0.3034	4.67
	0.2871	4.43	0.2839	4.38
	0.2826	4.40	0.2818	4.35
Chlorazene—Abbott (Baltimore)...	0.3496	5.38	0.2977	4.58
	0.3612	5.57	0.3027	4.65
	0.3477	5.35	0.2906	4.47
	0.3546	5.46	0.2956	4.54
Chlorazene—Abbott (Chicago).....	0.3498	5.40	0.2927	4.51
	0.3324	5.12	0.2785	4.28
	0.3348	5.15	0.2816	4.33
	0.3468	5.34	0.2961	4.56
Chlorazene—Abbott (New York)...	0.3472	5.35	0.2991	4.61
	0.3484	5.37	0.2991	4.61
	0.3450	5.32	0.2977	4.58
	0.3462	5.33	0.2991	4.61

Chloramine-T Surgical Paste (or Cream). — Chloramine-T Surgical Paste is claimed to consist essentially of 1 gram of Chloramine-T in 100 grams of a base composed approximately of sodium stearate 15 per cent. and water 85 per cent. Three market specimens each of "Chlorazene Surgical Cream" and "Chloramine-T Surgical Paste" were analyzed as follows:

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[11] In previous editions of "N. N. R.," the limits of water were 17 to 20 per cent., and of chlorine (Cl^+) from 11.5 to 13.0. On the recommendation of the manufacturers and after consultation the standards were made more stringent: the lower water limit raised to 18 per cent., and the lower chlorine limit raised to 12.0 per cent. The market supply is more in keeping with the old standards than with the revised standards.

Chloramine-T Paste—Squibb (Baltimore)	0.83% Chloramine-T[12] 0.81% Chloramine-T
Chloramine-T Paste—Squibb (Chicago)	1.05% Chloramine-T 1.03% Chloramine-T
Chloramine-T Paste—Squibb (New York)	1.01% Chloramine-T 1.00% Chloramine-T
Chlorazene Surgical Cream (Baltimore)	1.10% Chloramine-T 1.18% Chloramine-T
Chlorazene Surgical Cream (Chicago)	1.12% Chloramine-T 1.17% Chloramine-T
Chlorazene Surgical Cream (New York)	1.14% Chloramine-T 1.19% Chloramine-T

The variations are not as much as might be expected from a product containing so much water and organic matter. This fact illustrates how a slight alkalinity preserves the Chloramine-T.

Aromatic Chlorazene Powder-Abbott.—According to New and Nonofficial Remedies, "Aromatic Chlorazene Powder-Abbott" is composed of "chlorazene 5 per cent., sodium bicarbonate 5 per cent., eucalyptol 2 per cent., saccharin 1 per cent. and sodium chloride 87 per cent." Three market specimens

Analyses of Aromatic Chlorazene Powder

	Weight of Sample	Weight of Chloramine-T	Per Cent.
(Baltimore)	7.6579	0.3511	4.59
	10.5332	0.4923	4.65
(Chicago)	5.7615	0.2706	4.69
	7.3941	0.3476	4.70
(New York)	8.0189	0.3070	3.83
	7.6588	0.2935	3.83

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[12] Five to ten grams of the paste were transferred to a glass-stoppered Erlenmeyer flask and accurately weighed. Twenty c.c. of chloroform, 20 c.c. of potassium iodide solution (10 per cent.), 70 c.c. of water and 30 c.c. of acetic acid U. S. P. were added in the order named. The mixture was shaken until the paste had been entirely broken up, then titrated with tenth-normal sodium thiosulphate, using starch solution as indicator.

were analyzed the amount of Chloramine-T present being calculated from the reactive chlorine (Cl^+).

Thus in case of Samples 1 and 2, the amount of Chloramine-T found is only 8 per cent. below the amount claimed whereas in Sample 3, the amount is 25 per cent. less than claimed. This result is probably due to poor mixing since the product is quite stable as will be shown later.

Chlorazene Surgical Powder.—This substance is composed of "Chlorazene (Chloramine-T) 1 per cent., zinc stearate 10 per cent. and sodium stearate 89 per cent." Three specimens were analyzed.

Analyses of Chlorazene Surgical Powder

	Weight of Sample	Weight of Chloramine-T	Per Cent.
(Baltimore)................	8.6154	0.0803	0.93
	8.7700	0.0811	0.92
(Chicago)..................	9.2089	0.1182	1.28
	9.8076	0.1296	1.31
(New York)................	10.6416	0.0098	0.08
	9.8875	0.0084	0.08

This product shows considerable variation—from 30 per cent. over the claimed amount to 92 per cent. below. (A sample, previously unopened, received in 1917 contained no Chloramine-T.) It is evident that certain conditions arise which cause the Chloramine-T to decompose. The product cannot be considered satisfactory from a standpoint of stability.

PURITY OF MARKET SUPPLY OF DICHLORAMINE-T

As in the case of Chloramine-T, the essential standards for the purity of Dichloramine-T, para-toluene sulphone dichloramid $\left[CH_3C_6H_4SO_2N\left\langle\begin{matrix}Cl^+\\Cl^+\end{matrix}\right.\right]$, are described in New and Nonofficial Remedies. The determinations reported in this paper are (1) melting (decomposition) point and (2) chlorine content ("active chlorin").[13] The specimens were bought at the same time and in the same method as described under Chloramine-T.

Dichloramine-T Powder.—Of the eight specimens examined (the melting points and the chlorine determinations are given in Table III), all of them came well within the standards prescribed in New and Nonofficial Remedies except one sample of the Squibb product purchased in Chicago; in the latter case the melting point was quite low indicating decomposition, and the chlorine content was substandard; as might have been expected free hydrogen chloride was very per-

TABLE III.—*Dichloramine-T (Powder).*[14]

Brand	Melaing Point	Chlorin (Cl+) Content
Dichloramine-T—Abbott (Baltimore).......	79-80	28.86%
		29.08
Dichloramine-T—Abbott (Chicago).........	81-82	29.28
		29.33
Dichloramine-T—Abbott (New York).......	81-82	29.24
		29.41
Dichloramine-T—Monsanto (Baltimore)....	80-82	29.27
		29.29
Dichloramine-T—Monsanto (Sargents).....	79-81	29.18
		29.18
Dichloramine-T—Squibb (Baltimore)......	78-80	28.80
		28.78
Dichloramine-T—Squibb (Chicago).........	68-69	25.52
		25.70
Dichloramine-T—Squibb (New York).......	77-79	28.85
		28.86
"N. N. R." requirement...	78-83	28-29.5

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[13] The chlorine (Cl+) deetermination is carried out according to the "N. N. R." method: About 0.1 gram of Dichloramine-T, accurately weighed, is dissolved in 5 c.c. of glacial acetic acid, 10 c.c. of 10 per cent. aqueous solution of potassium iodide added and the mixture titrated with tenth-normal sodium thiosulphate. (If the reagents used liberate iodine, the number of cubic centimeters of tenth-normal sodium thiosulphate volumetric required for their decoloration, as determined by a control, should be deducted from the total volume used.) The chlorine content should not be higher than 29.53 per cent. or lower than 28 per cent. Each cubic centimeter of thiosulphate solution is equivalent to 0.00177 gram of chlorine.

[14] The McNeil brand is also described in "New and Nonofficial Remedies." However, our buyers were not able to supply the product. On inquiry, the firm gave the information that their product was sold almost entirely to dispensing physicians, hence, it was not found in the regular drug trade channels.

ceptible; the other Squibb specimens were of good order. Except for this one instance, the products are all quite satisfactory.

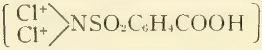
Dichloramine-T Tablets.—Only one firms' tablets have been described in New and Nonofficial Remedies, namely, the Abbott brand. Three original specimens were examined. (See results in Table IV.) The tablets (claimed to contain 4.6 grains Dichloramine-T) are uniform in weight and are within the variations accepted in this form of medication.

TABLE IV.—"*Tablets Dichloramine-T—Abbott, 4.6 Grams*"

	Weight of Tablets		Dichloramine-T	
	Grams	Grains	Grams	Grains
1. Baltimore...............	0.2950	4.55	0.2916	4.49
	0.3006	4.63	0.2976	4.58
	0.3014	4.65	0.2976	4.58
	0.2975	4.59	0.2934	4.50
2. Chicago.................	0.2953	4.55	0.2922	4.50
	0.3047	4.69	0.3012	4.64
	0.3025	4.66	0.3000	4.63
	0.2983	4.59	0.2928	4.50
3. New York...............	0.3000	4.63	0.2970	4.58
	0.2920	4.50	0.2895	4.47
	0.2958	4.56	0.2916	4.49

PURITY OF THE MARKET SUPPLY OF HALAZONE

Halazone is used almost exclusively in the form of tablets, containing a mild alkaline substance in which the halazone dissolves when water is treated with the tablet. The powder is, therefore, not carried by some firms in regular stock. The specimens received by us from the drug house bore only typewritten labels; in case of one firm no specimen was obtained. The essential standards of purity are the melting point or rather decomposition point and the chlorine (Cl^+) content.[15] Halazone is para-dichloramidosulphone benzoic acid



$\left[\begin{matrix}Cl^+\\Cl^+\end{matrix}\!>NSO_2C_6H_4COOH\right]$.

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[15] The following method for chlorine (Cl^+) determination is detailed in "New and Nonofficial Remedies:" About 0.150 gram of halazone (or in the case of halazone tablets, 30 tablets), accurately weighed, is dissolved in from 50 to 100 c.c. of water and 10 c.c. of a 10 per cent. sodium hydroxide solution. Fifteen cubic centimeters of a 10 per cent. potassium iodide solution are added, and the mixture titrated with tenth-normal sodium thiosulphate volumetric solution. (If the reagents used

Halazone Powder.—The products of two firms were examined:

Brand	Decomposition Point	Chlorin (Cl+) Content
Halazone—Abbott (Chicago)	195	22.96
		23.14
Halazone—Abbott (New York)	194	22.92
		23.11
Halazone—Monsanto	190	24.08
		24.08
"N. N. R." requirement	...	20 to 26.2

The Abbott products are slightly low in chlorine content; the one specimen of Monsanto product is just inside the chlorine (Cl^+) limits.

Halazone Tablets.—The tablets of two firms are listed in New and Nonofficial Remedies—"Abbott" and "Squibbs." Each tablet is claimed to contain 0.004 gram (1/16 grain) of halazone, 0.004 gram of sodium carbonate, and approximately 0.1 gram of sodium chloride. Chlorine (Cl^+) determinations yielded the following results, calculated to halazone:

	Amount of Halazone in Each Tablet
Halazone tablets—Abbott (Chicago)	0.0030 gram
	0.0030 gram
Halazone tablets—Abbott (New York)	0.0035 gram
	0.0035 gram
Halazone tablets—Squibb (Baltimore)	0.0033 gram
	0.0032 gram
Halazone tablets—Squibb (Chicago)	0.0030 gram
	0.0030 gram
Halazone tablets—Squibb (New York)	0.0034 gram
	0.0033 gram

The five specimens reported above are 12.5 to 25 per cent. below the amount of halazone claimed; considering how the compound is used, however, the variations are not therapeutically serious.

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liberate iodine, the number of cubic centimeters of tenth-normal sodium thiosulphate volumetric solution requires for their decolorization should be deducted from the total volume used.) The available chlorine content of halazone should not be higher than 26.26 per cent. or lower than 24 per cent. Each cubic centimeter of tenth-normal thiosulphate volumetric solution is equivalent to 0.00177 grams of chlorine. The theoretical chlorine content of pure halazone is 26.26 per cent.

TABLE V.—*Stability of "Chloramines"*

		Decomposition Point	Moisture	Chlorine (Cl^+)
Chloramine-T—Monsanto	Feb. 1918	164–166	18.46	11.94
	Sept. 1918	**163–164**	**16.61**	**11.9**
	July 1922	152	18.05	11.81
Chloramine-T—Calco	Oct. 1917	168–170	16.82	11.67
	Sept. 1918	**158–159**	**15.69**	11.8
	July 1922*	(See footnote)		
Chloramine-T—Squibb	June 1918	181	9.0	11.40
	Sept. 1918	**181**	**9.1**	**11.2**
	July 1922	173	9.2	11.1
Chlorazene—Abbott †	July 1916	Notes	Misfiled	.....
(Received July 5, 1916)	Sept. 1918	163		**11.07**
	July 1922	163		11.00
Chlorazene Surgical Powder	....	.....		0.00
(Received Dec., 1917)				(July 1922)
Aromatic Chlorazene Powder	....	.....		4.72
(Received August, 1919)				(July 1922)
Dichloramine-T—Abbott	Sept. 1918	**76–78**		**27.62**
(Received Oct., 1917)	July 1922	68–72		26.51
Dichloramine-T—Calco	Nov. 1917	81-82		28.6
	Sept. 1918	**75–77**		**27.9**
	July 1922	71–73		26.4
Dichloramine-T—Monsanto	Feb. 1918	80–82		29.2
	Sept. 1918	**77–79**		**28.6**
	July 1922	72–74		27.6
Dichloramine-T—Squibb	June 1918	77–79		29.00
	Sept. 1918	**76–79**		**28.3**
	July 1922	67–69		25.0
Halazone—Abbott	Aug. 1917	196		25.9
	July 1922	192		24.4
Halazone—Calco	Dec. 1917	195		25.9
	Sept. 1918	200		**25.8**
	July 1922	204		25.0
Halazone—Monsanto	Dec. 1917	...		24.9
	Sept. 1918	**198**		**24.2**
	July 1922	204		24.1
Halazone—Squibb	July 1918	204		24.0
	Sept. 1918	...		**23.8**
	July 1922	202		23.2

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* The Calco specimen of Chloramine-T—Calco was sent in a colorless glass container, and kept as the other specimens. On reexamination at this time ,it was found to be entirely decomposed, containing no reactive chlorin and melting at 122-123 C. All the other specimens were in dark glass as are the market specimens of Calco. This does not reflect against the Calco product, but the observation is of academic interest.

† Chlorazene was the first product on the American market. Several specimens were examined, at the request of the Committee on Synthetic Drugs, while the product was in the experimental stage. Then when the market specimen was submitted to the Council, it likewise was examined and found to be satisfactory. The exact figures on this latter specimen have been misfiled, but a chlorine determination on the sample was made by Mr. Rabak in 1918, as well as the recent one reported in this paper.

STABILITY OF THE CHLORAMINES

From the foregoing discussion, it is evident that Chloramine-T, Dichloramine-T and Halazone, as now found on the market, do not show serious deterioration in spite of the presence of the relatively unstable form in which the chlorine exists. This does not dispose of the question of stability over a period of years; so, it was opportune to reexamine samples analyzed when the products were first submitted to the Council and again examined during 1918 by Mr. William Rabak, at that time connected with the A. M. A. Laboratory. In the foregoing table (Table V) are given the dates of the analyses and the figures found in the order in which they were made. Those in boldface were by Mr. Rabak to whom credit is due. The specimens were kept in the dark, in their original containers, and at room temperature.

Decomposition of Solution of Aromatic Chlorazene Powder

Time	Per Cent.
1 hour	0.0
3 hours	0.7
1 day	2.7
3 days	5.0
8 days	7.0
23 days	14.0
4 months	37.0

It will thus be seen from Table V that samples of Chloramine-T, kept for about five years, show little deterioration. Dichloramine-T deteriorates somewhat, but the decomposition is not of a spontaneous nature. Halazone undergoes little change on standing. Chlorazene Surgical Powder probably does not keep over a long period, the sample (which had not previously been opened) having no Chloramine-T present; possibly the excipient had a slightly acid reaction hastening decomposition. On the other hand, aromatic Chlorazene Powder is stable; this is to be expected in view of the fact that it is an alkaline substance and hence the oxidizing power of Chloramine-T is lessened. Even solutions of Aromatic Chlorazene Powder deteriorate slowly when kept at room temperature exposed to indirect light over a period of weeks.

CONCLUSIONS

1. The oxidizing power of Chloramine-T is greatly lessened by slight increase in alkalinity of the solution. It is suggested that the bactericidal power may likewise be lessened in alkaline fluids and investigation is needed.

2. The market supply of Chloramine-T was examined. One Squibb specimen was below standard in both water and chlorine, and two Squibb specimens and Calco Chloramine-T did not contain a sufficient amount of water of crystallization. The Monsanto and Abbott products were satisfactory.

3. Chloramine-T Tablets of all firms described in New and Nonofficial Remedies were satisfactory.

4. Aromatic Chlorazene powder is stable.

5. Two samples of Chlorazene Surgical Powder (one recent and one old) were very poor; two others were satisfactory.

6 The market specimens of Chloramine-T pastes are satisfactory.

7. On the whole, the market specimens of Dichloramine-T —N. N. R. are satisfactory, as are the tablets.

8. The market specimens of Halazone examined were slightly substandard.

9. Halazone tablets over 12.5 per cent. to under 25 per cent. of the professed content were found.

10. Chloramine-T and Halazone are sufficiently stable to be kept over a period of five years. Dichloramine-T, on the other hand, decomposes slowly.

ADDENDA

The following editorial appeared in The Journal A. M. A., Aug. 18, 1923, p. 581.

THE CHLORIN ANTISEPTICS

During the Great War, when hypochlorite solutions came into wide use, their composition varied, owing chiefly to the lack of chemical control, and to the fact that formulas were changed a number of times. Finally, two or three years after their introduction, a standardized preparation—surgical solution of chlorinated soda[1]—was evolved. The essential attributes of this solution have been found to be (1) a definite alkalinity, mild in character (p_H 8 to 10); (2) hypertonicity, and (3) presence of the correct amount of sodium hypochlorite (from 0.4 to 0.5 per cent.). The success of treatment with this solution was dependent chiefly on good surgical technic coupled with rigorous laboratory control.

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[1] For the methods of preparation and the assay, see New and Nonofficial Remedies, 1923, p. 142.

Because the hypochlorite preparations in use were so unstable and existed only in solution, Dakin and his co-workers continued their researches, endeavoring to obtain other chlorin-bearing antiseptics which would not possess these two major disadvantages. The first one introduced was chloramin-T (sodium paratoluene-sulphochloramid); soon afterward followed the closely allied dichloramin-T and the water sterilizing agent halazone.[2] Both chloramin-T and dichloramin-T were favorably received as worth while additions to materia medica. The products have now been on the market for more than five years. Because they do contain the chlorin atom in its less stable modification, the composition and purity of the "chloramin" preparations have been watched carefully by the Chemical Laboratory of the American Medical Association. A recent report[3] from the laboratory deals with the examination of market specimens of the brands described in New and Nonofficial Remedies. Out of eight specimens of chloramin-T powder examined, one was considerably substandard, two were slightly substandard, and five were satisfactory. The chloramin-T tablets, chloramin-T pastes and an aromatic powder containing chloramin-T and sodium bicarbonate were satisfactory. Two out of four specimens of a surgical powder containing chloramin-T and zinc and sodium stearates were found to be quite decomposed. All of the market specimens of Council-accepted dichloramin-T complied with the standards. An investigation was also made of specimens which had been analyzed five years previously. The results showed that chloramin-T and halazone were sufficiently stable to be kept in solid form over a period of five years, whereas dichloramin-T decomposed slowly.

In comparing hypochlorite solutions (such as surgical solution of chlorinated soda-Carrel-Dakin) and the "chloramins," Dr. P. N. Leech, who made the examinations, points out that they have a common characteristic, namely, a positively charged chlorin atom; this relatively unstable atom (Cl^+) has a tendency to go over to the relatively more stable chlorid (Cl^-). Hence, the chloramins as well as the hypochlorite are active oxidizing agents. On this oxidation factor, Dr. Leech believes, depends the antiseptic or germicidal action of these preparations. Assuming this premise, the question arose as to what effect the reaction of the solution would have on the oxidizing power. Measurements of the oxidation potentials showed that the oxidizing power of chloramin-T was much greater in neutral than in even slightly alkaline solutions, and the power decreased with relatively small increase in alkalinity. Thus the statement is advanced that "it would not be surprising to find that the hydrogen ion concentration (C_H), the oxidation potential and the bactericidal coefficient would be in direct ratio." Therefore, one strength of a solution of pure chloramin-T might be active as a germicide in certain conditions, while a solution of the same strength containing sodium bicarbonate might be inadequate. As is suggested in the report, there is need for bacteriologic work to determine this factor.

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[2] Chloramin-T, dichloramin-T and halazone are described in New and Nonofficial Remedies, 1923, pp. 143-147.

[3] Leech, P. N.: Synthetic Drugs, IV, Examination of American-Made Chloramin-T, Dichloramin-T and Halazone, J. Am. Pharm. A. **12**: 592-602 (July) 1923.

THE CHEMICAL EXAMINATION OF SOME COMMERCIAL BRANDS OF CARBON TETRACHLORID

(Reprinted from The American Journal of Pharmacy, December, 1923, p. 864)

L. E. Warren, Ph.C., B.S.

The use of carbon tetrachlorid for the treatment of hookworm disease was first suggested by Maurice C. Hall,[1] of the Bureau of Animal Industry of the United States Department of Agriculture. For a number of years chloroform had been used as an anthelmintic against hookworms[2] and Hall was led to employ carbon tetrachlorid in experiments upon animals infected with hookworms because of its chemical relationship to chloroform, its higher boiling point and its scantier solubility in water. He gave the substance to dogs infected with hookworms and found that they tolerated the drug well, that toxic symptoms did not appear and that all of the hookworms present were removed, a result which he had never been able to accomplish by a single dose of any other anthelmintic. Hall also administered carbon tetrachlorid to horses and swine and found that it was very effective against the blood sucking strongyles and moderately effective against ascarids.

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[1] Hall, M. C.: J. Agr. Res. **21**: 157, 1921; ibid. **23**: 103, (1923; J. A. M. A. **77**: 1641, 1921; Am. J. Trop. Med. **2**: 373, 1922.

[2] Schultz, W. H.: J. A. M. A. **57**: 1102, 1911.

Experiments were also carried out on many other animals. In order to test its toxicity on man Hall swallowed 3 c.c. of the drug and experienced no symptoms except an eructation of carbon tetrachlorid and a slight sensation of warmth in the stomach which soon passed away. Because of the possibility of impurities Hall cautions that only a pure and carefully refined drug should be used. In collaboration with Hall, Lake[3] and Schillinger administered carbon tetrachlorid to monkeys. In general the results indicated that these animals might be given large and repeated doses of the drug without showing evidence of injury or lesions due to the drug on postmortem examination. In other words the drug was practically nontoxic in doses that were effective as a vermifuge. As a result of these experiments Hall concluded that carbon tetrachlorid was more effective in removing hookworms from animals than any of the other drugs commonly employed and that it was not only safe but much cheaper than other anthelmintics. Suggestions for its use in the treatment of hookworm disease in man naturally followed.

Apparently the first account of the use of carbon tetrachlorid in the treatment of hookworm disease in human beings was contained in a dispatch to the *London Times*[4] from the Fiji Islands in which the statement was made that in experiments upon coolies, 98 per cent. of the hookworms present were removed by a single dose of the substance. This work was afterward fully reported by Lambert.[5]

Encouraged by Hall's findings Leach[6] administered carbon tetrachlorid to fourteen volunteer prisoners, all but one of which were known to be infested with hookworms. Three weeks later all were negative to hookworm ova. To a condemned prisoner a dose of 10 c.c. was administered, followed in a week by 1 c.c. more. At necropsy, twenty-two days after the last treatment no hookworms were found but an enormous number (3,429) of oxyurids and thirty-two trichurids were found. The spleen was normal in size and consistency, the liver showed no lesions on microscopic examinatoin, and the kidneys were normal in appearance.

Acting on Hall's suggestion Nicholls and Hampton[7] administered carbon tetrachlorid to ninety-nine persons (mostly

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3. Lake, G. C.: Pub. Health Rep. **37**: 1123, 1922.
4. Dispatch, London Times, Feb. 11, p. 9, 1922.
5. Lambert, S. M.: J. A. M. A. **79**: 2055, 1922.
6. Leach, C. N.: J. A. M. A. **78**: 1789, 1922.
7. Nicholls, L., and Hampton, G. G.: Brit. M. J. **2**: 8, 1922.

children) most of whom were infected with hookworm and many with other helminths. These workers found the drug efficient for the removal of hookworm but not as effective as oil of chenopodium for the removal of ascaris.

McVail[8] reported on the use of carbon tetrachlorid in the treatment of hookworm disease in India. He and his assistants employed the drug alone and in admixture with castor oil and with oil of chenopodium. In sixty minim doses alone it appeared to be soporific but was without other untoward effects except in one very old man in which irregularity of the pulse and slurring speech were observed. When used alone the drug was completely effective in forty-one of fifty-one cases. The drug was effective in removing hookworms and threadworms but was not of much value against ascaris, trichuris and hymenolepsis. Because of the possibility that the drug might cause acute yellow atrophy of the liver McVail cautions against its employment as a routine, standard treatment until its limitations have been determined.

Lambert[5] administered carbon tetrachlorid to 20,000 patients in the Fiji Islands without a single death. He reported that the drug is a vermifuge and vermicide of great potency, that it gave but little discomfort, and that, because of its cheapness, it would permit the treatment at low cost of vast populations who were suffering from hookworm disease. From the standpoint of safety, efficiency and economy Lambert considered the remedy superior to chloroform, thymol or oil of chenopodium. It was not as effective as oil of chenopodium in removing ascarids or whip worms but it removed threadworms in large numbers.

In a latter paper,[9] Lambert reported treatment of an additional 30,000 cases but with three deaths and five other cases of serious illness. The first 42,000 cases were treated by Lambert with a certain lot of "carbon tetrachlorid which showed on analysis a small amount of carbon disulphid insufficient to do harm." No deaths or notable untoward symptoms were produced. The next 8,000 cases were treated by a different supply of carbon tetrachlorid. The three deaths and the cases of illness occurred in this group. The drug was examined and found to contain a considerable quantity of an unidentified impurity. At necropsy the liver in one case showed severe necrosis of the central and intermediate

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8. McVail, J. B.: Ind. M. Gaz. **57**: 290, 1922.

9. Lambert, S. M.: J. A. M. A. **80**: 526, 1923); ibid. **81**: 1553, 1923.

zones of the lobules. Many small, petechial hemorrhages were found under the capsule of the liver. Lambert believes that pure carbon tetrachlorid would not be toxic. In the latest work Lambert has given the carbon tetrachlorid mixed with a concentrated solution of magnesium sulphate. The results were better than when the purge was given three hours after the administration of the drug.

After learning of Hall's work, Smillie and Pessõa[10] in Sao Paulo found, that by giving a dose of 3 c.c. of carbon tetrachlorid divided into three hourly doses of 1 c.c each, 98 per cent. of the hookworms were removed by one treatment. Smaller doses were less effective. The male hookworms were more resistant to the treatment than the females. This differs from oil of chenopodium which has a greater toxicity to the male hookworm.[11] Smillie and Pessõa observed toxic effects in both dogs and man, the lesions being similar to those produced by chloroform. The symptoms were much worse in persons who were partially intoxicated with alcohol at the time of treatment. These workers conclude that carbon tetrachlorid in maximum doses of 3 c.c. is a reasonably safe treatment for hookworm disease.

Meyer and Pessõa[12] have studied the toxicity of carbon tetrachlorid on dogs. They found that the substance produced lesions in the liver and to a lesser extent in the kidneys. They found it to be a powerful vermifuge, but warned that it should be given with caution to human beings.

Love[13] treated ninety cases of hookworm mostly in children. Of these 82 per cent. were freed from infection by the first dose, 13 per cent required two doses and 4.4 per cent. three doses. Two of the children vomited the first dose. One patient who had been given over sixty doses of other anthelmintics (thymol; oil of chenopodium) was freed from hookworm by three doses of carbon tetrachlorid.

Docherty[14] has made a clinical comparison between thymol, betanaphthol, oil of chenopodium and carbon tetrachlorid, using 800 prisoners in order to insure absolute control of the patients while under treatment. The dose of carbon tetrachlorid employed was 3 c.c. followed in three hours by 50 c.c. of saturated solution of magnesium sulphate. The doses of the

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10. Smillie, W. G., and Pessôa, S. B.: Am. J. Hyg. **3**: 35, 1923.
11. Darling, S. T.; Barber, M. A., and Hacker, H. D.: Rep. Uncin. Com. Orient., p. 191, 1920.
12. Meyer, J. R., and Pessôa, S. B.: Am. J. Trop. M. **3**: 177, 1923.
13. Love, J. D.: J. Florida M. A. **9**: 176, 1923.
14. Docherty, J. M.: J. A. M. A. **81**: 454, 1923.

other drugs were such as are customarily employed as anthelmintics. By the method of comparison used and in the dosage employed, carbon tetrachlorid proved the most efficient of the four vermifuges tested both in the percentage of cures and in the percentage of total worms removed.

Because of the strong likelihood that carbon tetrachlorid would prove of value in medicine and because of the lack of standards for the identity and purity of the substance, the Council on Pharmacy and Chemistry took up its study with the view of its admission to New and Nonofficial Remedies. The literature of the chemistry of carbon tetrachlorid was studied in order to obtain information concerning the impurities which would most likely be present in the market product.

Carbon tetrachlorid is usually prepared by chlorinating carbon disulphid. Therefore the impurities most likely to be present in carbon tetrachlorid are free chlorin and carbon disulphid. The reports of chemical examinations of carbon tetrachlorid in the literature record the presence of carbon disulphid in several instances but none, apparently have recorded free chlorin as an impurity. Radcliffe[15] worked on known mixtures of pure carbon tetrachlorid and carbon disulphid, containing up to 16 per cent. of the latter subtsance. His method, which was an adaptation of Gastine's procedure,[16] consisted in converting the carbon disulphid into potassium xanthate by treatment with cold alcoholic potassium hydroxid solution, acidifying with acetic acid and titrating the liberated xanthic acid with tenth-normal iodin solution in presence of sodium bicarbonate, using starch solution as indicator. His results are given in Table 1 herewith:

TABLE 1.—*Analysis of Known Mixtures of Carbon Tetrachlorid and Carbon Disulphid*

CS_2 Added	CS_2 Found
0	0
3.89	3.81
5.53	5.42
8.96	8.94
11.3	11.3
16.00	15.88

In 1909, Waller[17] found that a sample of "hair wash," which had caused the death of a young woman on whom it had been used as a shampoo, and which was composed essentially of perfumed carbon tetrachlorid, was considerably more toxic to isolated muscle than a specimen of pure carbon tetrachlorid. Veley [18] found the impurity in this toxic "hair wash" to be chiefly carbon disulphid, of which he estimated about 1.5 per cent. to be present. His methods of separation depended on careful fractional distillation and were admitted not to be very accurate. Wilcox [19] testified that he had examined the shampoo above mentioned and that it contained in addition to carbon tetrachlorid, 2.4 per cent. of carbon disulphid and 1.4 per cent. of water.

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[15] Radcliffe, L. G.: J. Soc. Chem. Ind. **28:** 229, 1909.

[16] Gastine, G.: Compt. rend. **98:** 1588, 1884.

[17] Waller, A. D.: Lancet **177:** 369, 1909.

Chemical manufacturers were invited to submit specimens of their medicinal carbon tetrachlorid together with the tests and standards by which the identity and purity of their products might be determined The replies as first received indicated that none of the manufacturers listed brands of carbon tetrachlorid for medicinal use, but that several of them advertised a brand which had been prepared for reagent purposes and which was stated to be of a high degree of purity. Brands intended for medicinal use were submitted later. In addition to the specimens submitted by certain of the manufacturers, specimens were purchased on the market and two were received from government officials. One of these latter was sent by Dr. Hall of the Bureau of Animal Industry of the United States Department of Agriculture, and the other by Dr. Lake, of the Public Health Service. The specimen received from Dr. Hall was a portion of that used in his experiments in removing hookworms from lower animals mentioned earlier in this paper, and the specimen received from Dr. Lake was the portion remaining after his experiments on monkeys described earlier in this paper. As neither of these specimens had been tested for impurities, they were included in the examination. For the sake of comparison a specimen sold as "technical" was also included in the study.

Each of the specimens received was subjected to chemical examination. The tests included observation of the physical properties, such as color, specific gravity and boiling point, tests for acidity, chlorid, free chlorin, aldehyds, organic impurities and carbon disulphid and determination of the residue on evaporation. Some of the tests were suggested by the manufacturers and some were obtained from the

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18. Veley, V. H.: Ibid., 370.
19. Willcox, W. H.: Pharm. J. **83**: 457, 1909.

literature. The qualitative tests to which the specimens were subjected are as follows:

Shake 10 c.c. of carbon tetrachlorid with 10 c.c. of water. The aqueous layer should be neutral to litmus paper and should not give an opalescence with silver nitrate solution *(chlorids)*.

Shake 10 c.c. of carbon tetrachlorid with 10 c.c. of water containing a few drops of potassium iodid solution. On standing for five minutes the lower layer should not be colored violet *(free chlorin)*.

Warm 10 c.c. of carbon tetrachlorid with 10 c.c. of 25 per cent. potassium hydroxid solution. No yellow or brown color should develop (*aldehyds*).

Mix 10 c.c. of carbon tetrachlorid with 10 c.c. of sulphuric acid and shake occasionally for five minutes. Not more than a barely perceptible color should be present in either layer *(organic impurities)*.

Mix 10 c.c. of carbon tetrachlorid with 10 c.c. of half-normal alcoholic potassium hydroxid solution and shake at intervals for two hours. Add 10 c.c. of water and shake again. Draw off as much of the aqueous layer as possible and acidify slightly with diluted acetic acid. Add a few drops of copper sulphate solution. No precipitate should form *(carbon disulphid)*.

None of the specimens examined gave any weighable residue on evaporation, and none responded to the tests for chlorids, free chlorin, aldehyds or organic impurities. Most of the specimens responded to the tests for carbon disulphid. Since, as previously mentioned, carbon tetrachlorid may be made from carbon disulphid this substance may be found in commercial specimens of the drug. Because of the toxic properties of carbon disulphid its presence in any considerable amount in carbon tetrachlorid intended for medicinal use would be undesirable. Carbon disulphid was determined quantitatively in such of the specimens as were found to contain it. Several methods have been suggested for determining carbon disulphid in benzene, carbon tetrachlorid. etc. The method used in this study is an adaptation of that published by Weiss[20] for the determination of carbon disulphid in benzene. As carried out in this laboratory the method is as follows:

About 5 gm. of the material are weighed, placed in a reflux apparatus with 20 c.c. of half-normal alcoholic potassium hydroxid solution and the mixture gently boiled for thirty minutes. The solution is diluted with 50 c.c. of water and 3 c.c. of 20 per cent. alcoholic potassium hydroxid solution, the mixture warmed on the steam bath until the carbon tetrachlorid and alcohol have been removed and 50 c.c. of bromin water are added gradually to the alkaline solution. (An excess of bromin water must be used.) After warming for fifteen minutes an excess of hydrochloric acid is added and the solution filtered. An excess of barium chlorid solution is then added and the barium sulphate collected, heated and weighed in the usual way.[21]

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[20] Weiss, J. M.: J. Ind. Eng. Chem. **1**: 604, 1909.

$$BaSO_4 \times 0.16308 = CS_2$$

The findings from the several determinations are tabulated herewith:

TABLE 2.—*Analyses of Carbon Tetrachlorid*

Brand	Sp. Gr. 25°/25°	Boiling Point	Carbon Disulphid	Claims
P. W. R. Analytical Chemicals (Hall)......................	1.5887	76-76.2°	0.086	CS_2 0.1%
P. W. R. Analytical Chemicals (fr. Mfr.)..................	1.5897	76.4°	None	CS_2 none
Baker's Analyzed (Lake)......	1.5886	76-76.2°	0.213	S comp. none
Baker's Analyzed (Purchased)	1.5888	76°	0.096	S comp. none
Central Scientific (Purchased)	1.5888	76-76.2°	0.052	C. P.
M. C. W. Technical (Purchased)	1.5879	75.9-76.2°	0.223	Technical
M. C. W. Redistilled (fr. Mfr.)..	1.5888	....	0.108	Pure redistilled
M. C. W. Medicinal (fr. Mfr.)...	1.58895	76-76.2°	0.015	C. P. medicinal
H. K. Mulford capsules (fr. Mfr.)......................	......	....	0.271	

A comparison of these results with the meager reports of earlier examinations indicates that the brands of carbon tetrachlorid of the present market are of a greater degree of purity than they formerly were. They indicate, too, that manufacturers are making an effort to reduce the quantity of carbon disulphid in their products. For example, one specimen of the P. W. R. brand which was known to be at least one year old was admitted (by the label) to contain

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[21] In determining carbon disulphid a blank determination for sulphur was made in the reagents, using 20 c.c. of 2 per cent. alcoholic potassium hydroxid solution, 5 c.c. of 20 per cent. alcoholic potassium hydroxid solution, 100 c.c. of bromine water, 5 c.c. of hydrochloric acid, and 5 c.c. of barium chlorid solution. The barium sulphate found weighed 0.0022 gm. This correction was, therefore, applied to all weights of barium sulphate obtained.

0.1 per cent. of carbon disulphid, whereas a recent specimen contained none. One specimen of the Baker's analyzed brand which was at least one year old and which was claimed to contain no sulphur compounds, was found to contain over 0.2 per cent. of carbon disulphid. In a recent specimen the amount of this impurity had been reduced to less than 0.1 per cent. although the label still declared sulphur compounds to be absent. As long ago as 1914, Lehner[22] pointed out that reliance could not be placed on the claims made for "Analyzed Chemicals." The specimen from H. K. Mulford and Company was in the form of capsules. The content of the capsules was very high in sulphur. No specimen of carbon tetrachlorid Mulford was received in bulk so that no judgment could be made concerning the purity of the carbon tetrachlorid originally used in preparing the capsules.

Based upon the results of this examination, standards for the identity and purity of carbon tetrachlorid were adotped by the Council on Pharmacy and Chemistry which required a clear, colorless liquid, having a specific gravity of not less than 1.588 at 25 C./25 C., which should be free from chlorids, free chlorin, aldehydes and organic impurities, which should not give more than 0.001 gm. of residue from 25 c.c. on evaporation, and which should not contain more than 0.1 per cent. of carbon disulphid.

The description for carbon tetrachlorid as adopted by the Council on Pharmacy and Chemistry for New and Nonofficial Remedies is as follows:

CARBON TETRACHLORID MEDICINAL. — Carbonei tetrachloridum medicinale.—Tetrachlormethan.—CCl_4.

Actions and Uses.—Carbon tetrachlorid has narcótic and anesthetic properties somewhat similar to those of chloroform. It has recently come into use as a vermifuge in the treatment of hookworm disease. It also removes some intestinal parasites other than the hookworm, such as *Oxyuris vermicularis*, *Ascaris lumbricoides* and *Trichocephalus dispar*, but it is less effective against these worms than some other drugs, such as oil of chenopodium. It is reported that usually about 85 per cent. of the hookworms are removed by the first dose of carbon tetrachlorid and that occasionally all are removed. As a vermifuge it appears to be relatively safe, but serious symptoms and even death have been reported, especially in patients addicted to the use of alcohol. The best results are obtained by administration in water or milk or in gelatin capsules on an empty stomach, followed in 3 hours by a purgative dose of magnesium sulphate. The capsules may be prepared extemporaneously. A mild laxative is generally given to constipated patients on the day previous to treatment. To insure complete removal of the hookworms, a test dose of oil of chenopodium, 3 c.c. (45 minims) may be given a week after the treatment with carbon tetrachlorid. A second dose of carbon tetrachlorid medicinal should not be given within three weeks. Alcohol should not be taken during treatment.

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[22] Lehner, V.: J. Ind. Eng. Chem. **6:** 603, 1914.

Dosage.—From 2 to 3 c.c. (30 to 45 minims). Children 0.13 c.c. (2 minims) for each year of age up to fifteen years. The dose of 3 c.c. should not tbe exceeded.

Carbon tetrachlorid is a clear, colorless, mobile liquid, having a characteristic, ethereal odor somewhat like that of chloroform; almost tasteless. Carbon tetrachlorid is almost insoluble in water and glycerin; miscible with alcohol, chloroform, petroleum benzin and benzene; also soluble in most of the fixed and volatile oils. Specific gravity not less than 1.588 at 25 C. Carbon tetrachlorid is volatile at ordinary temperature, but is not inflammable. Medicinal carbon tetrachlorid boils at from 76 to 77 C.

Shake 10 c.c. of carbon tetrachlorid medicinal with 10 c.c. of water; the aqueous layer should be neutral to litmus paper and should not give an opalescence with silver nitrate solution (*chloride*). Shake 10 c.c. of carbon tetrachlorid medicinal with 10 c.c. of water containing a few drops of potassium iodid solution; on standing for five minutes the lower layer should not be colored violet (*free chlorin*). Warm 10 c.c. of carbon tetrachlorid medicinal with 10 c.c. of 25 per cent. potassium hydroxid solution; no yellow or brown color should develop (*aldehyds*). Mix 10 c.c. of carbon tetrachlorid medicinal with 10 c.c. of sulphuric acid and shake occasionally for 5 minutes; not more than a barely perceptible color should be present in either layer (*organic impurities*).

Evaporate 25 c.c. of carbon tetrachlorid medicinal almost to dryness in a weighed dish on a steam bath. Allow the remainder to evaporate spontaneously. The residue, if any, should be odorless. Dry the residue at 100 C. and weigh. The residue should not weigh more than 0.001 gm. About 5 gm. of carbon tetrachlorid medicinal are weighed, placed in a reflux apparatus with 20 c.c. of half-normal alcoholic potassium hydroxid and the mixture gently boiled for 30 minutes. The solution is diluted with 50 c.c. of water and 5 c.c. of 20 per cent. alcoholic potassium hydroxid solution, the mixture warmed on the steam bath until the carbon tetrachlorid and alcohol have been removed and 50 c.c. of bromin water are added gradually to the alkalin solution. (An excess of bromin water must be used.) After warming for 15 minutes an excess of hydrochloric acid is added and the solution filtered. An excess of barium chlorid solution is then added and the barium sulphate collected, heated and weighed in the usual way. The weight of barium sulphate obtained should correspond to not more than 0.1 per cent. of carbon disulphid.

PART II

REPORTS BASED ON ARTICLES WHICH APPEARED IN THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION AND IN HYGEIA

QUAYLE'S "BOB-WHITE HABIT SINKERS"

An Alleged Cure for Morphinism and Other Drug Addictions

Extracted from The Journal A. M. A., Jan. 27, 1923, p. 270

Charles H. Quayle, M.D., of Madison, Ohio, "Medical Director" of the "Dr. Quayle Sanitarium, a Retreat for Drug Addicts, Alcoholics and Cigarette Inveterates" and "Specialist in Drug and Liquor Addictions" has for some years been exploiting an alleged cure for chronic morphinism "and any other drug addiction."

In 1914 Quayle was sending out to physicians from Madison, Ohio, a circular letter regarding the alleged wonders of "Dr. Quayle's Guaranteed Three Day Drug and Liquor Treatment." According to this letter, Quayle "by unremitting study, experiments and observation" had at last "discovered an absolute cure for the relief of the craving for *all Drugs and Liquors.*" Further, this alleged treatment was —at that time—"not for sale to any layman or person who wishes to treat himself;" it could "only be purchased by a Physician" and was "for the use and advantage of the medical profession only." The Quayle letter explained that the price of the treatment to the physician would be "$25.00 with the understanding that no Physician is to administer it for less than $50.00 per patient."

In March, 1915, Quayle was sending letters to sanatoriums from Cleveland, Ohio, and offering to license the physicians in charge so that their institutions could have a monopoly of the use of Quayle's treatment in a given "district."

Since 1915 Quayle has evidently changed his method of exploitation and the "medicine" that, at that time, was "not for sale to laymen or persons who wished to treat themselves" is now to be found advertised in the *Police Gazette, Smart Set,* etc.

One of Quayle's newspaper advertisements, "Morphin, New Home Treatment: Send Stamp for Book of Information" was answered and, in reply, came a form letter signed "Charles H. Quayle, M.D., Medical Director," stating that a booklet was enclosed and also a history blank that must be filled out when ordering treatment. The letter stated further that "the 'HARIT SINKERS' cause no pain, sickness, nor the loss of time; are harmless, contain no NARCOTICS or other habit-forming drugs and are easy to take." Moreover, it said that "the amount of Morphin or the length of time makes no difference"; it closed with the statement that the price of the treatment is $25.00 and "All treatments sent in plain packages."

Twenty-five dollars was sent to Quayle by a layman for one "treatment" which consists of four boxes of pills. One of the boxes contains three chocolate-coated pills and one capsule; another box contains twelve white-coated tablets; in a third are thirty-seven red-coated pills, while the fourth—the alleged "Antidote"—contains 323 yellow-coated tablets. A small leaflet accompanies the boxes, giving "Directions for Taking." The sufferer is told, first, to take the three chocolate-coated pills and the capsule and twelve hours later to "take two teaspoonfuls of Sal-Hepatica." He is told, further, that the bowels should move two or three times a day and, if necessary to accomplish this, one of the white-coated tablets should be taken each night at bedtime, followed the next morning by "two teaspoonfuls of Sal-Hepatica." He is warned tto "use no acids while taking medicine."

As the second step in the treatment the patient takes the yellow-coated tablets described as "Antidote." The sufferer is warned that should he "vomit or feel sick to stomach" or should he "experience seeing imaginary objects" the "Antidote" tablets should be discontinued until the symptoms have passed. He is also told not to attempt to read while taking these tablets "as pupils are dilated." Further, he is told that should "any nervousness or desire for morphin" be felt after the ninth day, the "Antidote" tablets should be continued "up to the 12th, 15th or 21st day or until you feel sure of yourself."

The tablets in the fourth box are to be taken, one after each meal, "after there is no more desire for morphin and you have finished with the antidote tablets." The patient is told, also, that while taking the treatment, the diet should consist of milk, cereals, eggs and vegetables only, and these taken sparingly and that glass of water should be taken every two hours.

The complete Quale treatment was turned over to the A. M. A. Chemical Laboratory for analysis. The laboratory reported as follows:

LABORATORY REPORT

One original package of "The Quale Treatment" (Dr. Quayle Sanitarium, Madison, Ohio) was submitted to the chemical laboratory for examination. The package consisted of a box in which were four smaller boxes labeled as follows:

"*No. 1.—Eliminative.*" (Contained 3 chocolate-coated pills and 1 capsule.)

"*No. 2.—Antidote.*" (Contained 323 yellow-coated tablets.)

"*No. 3.—Nerve Tonic.*" (Contained 37 red-coated pills.)

"*Special Eliminative Bowel Tablets.*" (Contained twelve white-coated tablets.)

The box "No. 1—Eliminative" contained three chocolate-coated pills and a capsule of grayish powder. The pills contained a soft mass which gave a positive reaction for emodin-bearing (laxative) drugs; mercurous chlorid (calomel) was absent. The capsule contained a gray powder of metallic mercury and excipients such as found in certain modifications of Mass of Mercury ("blue mass") and so-called "blue mass powder."

The box "No. 2—Antidote" contained 323 yellow-coated tablets which disintegrated in water with difficulty. These tablets contained, essentially, a laxative element such as cascara, and gave tests for atropin. Tests for strychnin, pilocarpin and scopolamin were negative. The atropin is probably incorporated in the form of an extract of belladonno.

Box "No. 3—Nerve Tonic" contained thirty-seven red-coated pills containing strychnin.

The box "Special Eliminative Bowel Tablets" contained twelve white-coated tablets. In these was found mercurous chlorid (calomel); they also yielded a positive test for emodin-bearing drugs.

Summed up, the "Quayle treatment" for "Morphin or Any Other Drug Addiction" is, essentially, (1) active elimination by cathartics; (2) the administration of atropin during the stage of morphin withdrawal and (3) the use of strychnin at the close of the "treatment."

In conclusion, The Journal stated: "It is evident from the laboratory findings that this alleged 'absolute cure,' said to have been discovered by Quayle 'after years of investigation and research' and 'by unremitting study, experiments and observations,' is no more a cure than could be devised by any physician who is familiar with modern medical literature. The analysis fails to show a single element of originality in it. The scheme of having a quantity of morphin equal to several days' dosage dissolved in water to be periodically diluted as the patient uses it, is one that has been tried and found wanting—for generations. No physician will believe that a patient suffering from chronic morphinism can cure himself by any such method as that exploited by Quayle. That an occasional morphinist might cease the use of the drug coincidentally with the taking of the Quayle treatment is conceivable, although inherently improbable. For the one individual who possesses the almost superhuman will-power to give up the drug to which he is enslaved while treating himself, there must be hundreds to whom any method of self-treatment must be a more or less brief period of physical agony followed by the almost inevitable relapse with the mental suffering that such a relapse implies. 'Play the game fair and do not cheat if you wish to win. . . . it will require some grit and will power on your part,' says Quayle in the letter that accompanies the $25.00 worth of pills. The ghastly irony of this exhortation will be understood by those who have seen the suffering of a morphinist even when being treated under ideal institutional surroundings."

ALLEN'S GOITER TREATMENT

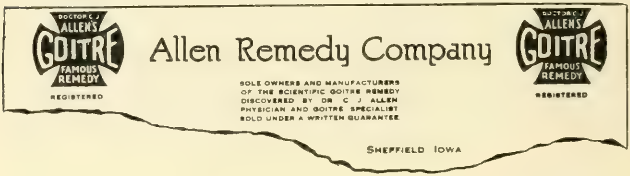
(Abstracted, with additions, from The Journal A. M. A., Feb. 24, 1923, p. 572)

At Sheffield, Iowa, the Allen Remedy Company conducts a mail-order business in "Dr. C. J. Allen's Goiter Treatment." Business is drummed up, apparently, by means of agents and traveling representatives. During the past few months several inquiries have been received about this product. We quote from some of them:

> "I have under my care a patient who had developed a toxic adenoma of the thyroid as a result of taking the Allen Goiter medicine made at Sheffield, Iowa. This patient was examined at our clinic some months ago and a clinical diagnosis was made of non-toxic, multiple adenomata. She now appears after having taken this medicine for several months with all the symptoms of thyrotoxicosis, including a basal metabolic rate of plus 44 per cent. She reports a neighbor who is in the same condition as herself as a result of taking this treatment. Dr. ——— of this city today told my brother of two cases coming to his attention in the past week, both of whom had been taking this treatment, and one of whom is so toxic that she may not live."

> "I wish to secure some information regarding the Allen Remedy Company of Sheffield, Iowa, and especially regarding Dr. C. J. Allen's Goiter Remedy put out by this company. Several patients of mine with different types of goiter have been solicited by a Mr. A. D. Tabor of Cedar Rapids, Iowa, and some of them have asked me for an opinion regarding it."
>
> "Under separate cover, I am mailing you a bottle of dope put out by the Allen Remedy Co. of Sheffield, Iowa. This has been sold in our community lately as a sure cure of goiter of all kinds. Can you enlighten me as to its relative merits for such a sure fire cure and also what the medicinal ingredients might be?"

According to the records in The Journal office, C. J. Allen of Sheffield, Iowa, died in August, 1917, of tuberculosis. He was graduated by Rush Medical College in 1887. The records fail to show that he was ever a member of his local medical society. The advertising matter put out by the Allen Remedy Company states that C. J. Allen "discovered" his cure some years ago, that its fame began to spread and as a result, "C. J. Allen became a goiter specialist and was recognized as such by many leading medical authorities." This statement, of course, is unqualifiedly false. A careful search of medical literature for thirty years past fails to show that C. J. Allen ever made a single contribution to scientific medical literature.



DOCTOR C J ALLEN'S GOITRE FAMOUS REMEDY
REGISTERED

Allen Remedy Company

SOLE OWNERS AND MANUFACTURERS
OF THE SCIENTIFIC GOITRE REMEDY
DISCOVERED BY DR C J ALLEN
PHYSICIAN AND GOITRE SPECIALIST
SOLD UNDER A WRITTEN GUARANTEE

DOCTOR C J ALLEN'S GOITRE FAMOUS REMEDY
REGISTERED

SHEFFIELD IOWA

The "treatment" consists of sixteen four ounce bottles of the preparation, for which $90.00 is charged. Those using the product are told to take a teaspoonful with water after each meal. They are especially instructed to "massage the goiter both morning and evening" and, in black-faced type, are told that "This is very important."

Some original specimens of the Allen nostrum were secured, submitted to the Chemical Laboratory for analysis and the following report published in The Journal.

"Allen's Goiter Treatment is a reddish-brown, syrupy liquid having an acid reaction and an odor of sassafras and wintergreen. No information is given by the manufacturers concerning the composition of the preparation except that the presence of 4 per cent. of alcohol is declared. Alkaloids, benzoates, salicylates, glycerin, emodin-bearing drugs, potassium salts, sodium salts, and calcium salts are absent, or present only in traces. Qualitative tests demonstrate the presence of an ammonium salt in very small amounts, an iron salt (in the ferrous state), iodid ions, sucrose (cane sugar), small quantities of a phosphate, coloring matter and alcohol. The iodid is present partly as ferrous iodid and partly as free hydrogen iodid. The ammonia, the iron and the iodin were determined separately. The iron found was equivalent to about 0.83 gm. of ferrous iodid per 100 c.c. The ammonia found was equivalent to about 0.06 gm. of ammonium iodid per 100 c.c. and the hydrogen iodid was equivalent to about 1.74 gm. per 100 c.c. The alcohol content was 3.98 per cent. Each fluid dram (teaspoonful) of this preparation, therefore, contains approximately 1 grain of hydriodic acid and one-half grain of ferrous iodid.

"From the results obtained it is concluded that Allen's Goiter Treatment consists essentially of ferrous iodid and hydrogen iodid (hydriodic acid) in a colored and flavored syrup."

THE JOURNAL commented on the nostrum as follows:

The profits made from selling four pints of a syrup of ferrous iodid and hydriodic acid for $90.00 must surely not be inconsiderable. This, however, is a minor indictment. The most serious feature of the business is the viciousness of the indiscriminate sale of an iodid mixture to those who may be and are likely to be suffering from exophthalmic goiter. Add to this the pernicious suggestion that the victim should massage the thyroid daily and it is not surprising that physicians are beginning to report serious results from the use of this preparation.

Details of Analysis

Alcohol.—This was determined by the official method of the A. O. A. C., 50 c.c. being distilled to 100 c.c. The specific gravity of the distillate was 0.99702 at $\frac{15.6\text{ C.}}{15.6\text{ C.}}$ corresponding to 3.98 per cent. of alcohol by volume in the original material.

Ammonium Iodid.—To 50 c.c. of the material a slight excess of potassium hydroxid solution was added and the mixture distilled into a measured excess of normal hydrochloric acid. The excess of acid was titrated with tenth-normal potassium hydroxid, using alizarin red as an indicator. The ammonia present was calculated from the amount of normal hydrochloric acid consumed. The ammonia from 50 c.c. of material required 0.243 c.c. of normal hydrochloric acid, equivalent to 0.0704 gm. of ammonium iodid per 100 c.c. of original material. A duplicate of 50 c.c. consumed 0.167 c.c. of normal hydrochloric acid, equivalent to 0.0483 gm. of ammonium iodid per 100 c.c. Average, 0.059 gm. of ammonium iodid per 100 c.c.

Ferrous Iodid.—A measured portion of the solution was heated with a mixture of sulphuric and nitric acids until all of the organic matter had been destroyed, after which the resulting solution was diluted to 1,000 c.c. An aliquot portion (250 c.c.) of this solution, representing 12.5 c.c. of the original, was evaporated to small volume, made alkaline with ammonium hydroxid, the iron hydroxid (and phosphate) collected on a filter. The precipitate was washed with water, dissolved in dilute hydrochloric acid, 5 c.c. of potassium iodid solution were added and the liberated iodin titrated with tenth-normal sodium thiosulphate solution in the usual way. The iron from 12.5 c.c. of original material required 6.6 c.c. of tenth-normal sodium thiosulphate solution, equivalent to 0.8176 gm. of ferrous iodid per 100 c.c. A duplicate of 100 c.c. (representing 5 c.c. of original material) required 2.7 c.c. of tenth-normal sodium thiosulphate solution equivalent to 0.8361 gm. of ferrous iodid per 100 c.c. Average, 0.827 gm. of ferrous iodid per 100 c.c.

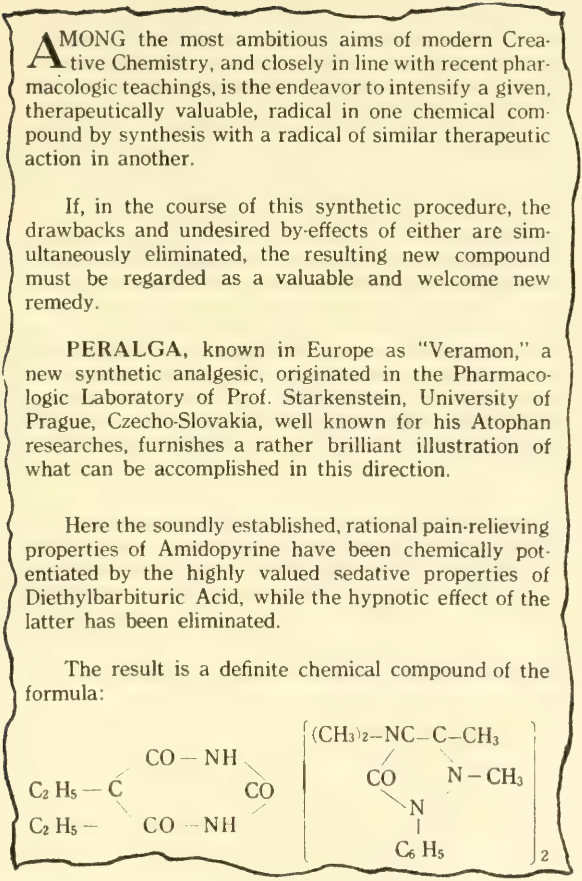
Hydrogen Iodid.—This was determined by direct titration of the material with tenth-normal sodium hydroxid solution, using phenolphthalein as indicator. The acidity of 100 c.c. of diluted material, representing 8 c.c. of original material, required 10.89 c.c. of tenth-normal sodium hydroxid solution, equivalent to 1.74 gm. of hydriodic acid per 100 c.c. of original material. A duplicate required the same amount of standard alkali as the first.

PERALGA

A New Foreign "Synthetic"

(Reprinted from The Journal A. M. A., March 31, 1923, p. 942)

For the past few years, American physicians have been relatively free from the propaganda of the foreign synthetic drugs—real or alleged. Recently, however, there have been signs of a revival of this type of product. One of the prod-



AMONG the most ambitious aims of modern Creative Chemistry, and closely in line with recent pharmacologic teachings, is the endeavor to intensify a given, therapeutically valuable, radical in one chemical compound by synthesis with a radical of similar therapeutic action in another.

If, in the course of this synthetic procedure, the drawbacks and undesired by-effects of either are simultaneously eliminated, the resulting new compound must be regarded as a valuable and welcome new remedy.

PERALGA, known in Europe as "Veramon," a new synthetic analgesic, originated in the Pharmacologic Laboratory of Prof. Starkenstein, University of Prague, Czecho-Slovakia, well known for his Atophan researches, furnishes a rather brilliant illustration of what can be accomplished in this direction.

Here the soundly established, rational pain-relieving properties of Amidopyrine have been chemically potentiated by the highly valued sedative properties of Diethylbarbituric Acid, while the hypnotic effect of the latter has been eliminated.

The result is a definite chemical compound of the formula:

Photographic reproduction (reduced) of part of a Peralga advertising circular. Note the formidable structural formula (alleged) reminiscent of a decade ago.

ucts now being endowed with the halo of creative chemistry is Peralga (Schering & Glatz), known in Europe as Veramon. But let Schering & Glatz describe the new creation—the new chemistry (according to S. & G.) "to intensify a given, therapeutically valuable, radical in one chemical compound by snythesis with a radical of similar therapeutic action in another:"

> "Peralga, known in Europe as 'Veramon,' a new synthetic analgesic, originated in the Pharmacologic Laboratory of Prof. Starkenstein, University of Prague, Czecho-Slovakia, well known for his Atophan researches, furnishes a rather brilliant illustration of what can be accomplished in this direction."

Incidentally it might be said that Starkenstein has lent his name to a number of statements valuable to the proprietary interests, but which cannot stand scientific light.

Peralga, it is claimed, is a "definite chemical compound," the alleged structure of which appears in the accompanying illustration reproducing a page from an advertising circular. According to Starkenstein Peralga is made by heating a mixture of diethylbarbituric acid (barbital) and amidopyrin (first introduced as "Pyramidon"). It is also claimed that Peralga is absorbed without being split up into its component radicals.

To a chemist, this new "synthetic" resembles a mixture more than it does a compound; it is reminiscent of the days of fake synthetics Consequently the A. M. A. Chemical Laboratory investigated Peralga. The product is a yellow powder with a methylamine-like odor. It is claimed to melt at 95-97 C., to be readily soluble in hot water and organic solvents, less soluble in cold water. As already mentioned it s said to be formed by heating a mixture of barbital and amidopyrin until fusion takes place.[1]

That Peralga is *not* a "definite chemical compound" as claimed will be seen from what follows: When Peralga is treated with water, or 0.2 per cent. hydrochloric acid solution, in sufficient quantity easily to dissolve the theoretical amount of amidopyrin, an insoluble substance can be removed. The latter has the melting point of barbital and when mixed with a known specimen of barbital, the melting point is not depressed thus identifying it as barbital. In common with barbital, Peralga is more soluble in sodium bicarbonate solution than in water. It is readily soluble in sodium hydroxid solution. Some Peralga was dissolved in sodium hydroxid solution, and shaken, in a separator with chloroform, the chloroform extract was evaporated to dryness in a current of warm air. The substance melted at 103 C. to 105 C., a mixture of the substance and amidopyrin melted at 105 C. to 107 C., and the amidopyrin control melted at 107-108 C. This shows the extracted substance to be practically pure amidopyrin. Quantitatively the amount of barbital extracted from Peralga was 26.1 per cent. and the amidopyrin extracted was 72.0.

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[1] If barbital or amidopyrin is placed in an oven at 100 C., no apparent change takes place; but when mixed fusion occurs (such as happens in a depressed melting point determination), with formation of yellow color and amine odor. In this manner there is formed a relatively small amount of a decomposition product, or probably products, not identified.

Evidently, then, Peralga is not a "definite chemical compound." From a chemical viewpoint it seemed improbable that Peralga (a fusion mixture of barbital and amidopyrin with some decomposition product) will produce any effect different from a mechanical mixture of barbital and amidopyrin in the same proportions.

To determine this, a mechanical mixture of barbital and amidopyrin in the same proportion as in Peralga and also some original Peralga were sent to the Pharmacologic Laboratory of Cornell University Medical College for comparative tests. The summary of the Cornell laboratory report was:

> "We can see no difference in the behavior of cats toward similar doses of the two preparations: the mechanical mixture made in the A. M. A. Chemical Laboratory and the preparation of Schering & Glatz—and they show very little difference between similar doses of barbital and those contained in Peralga. . . . Of course, there is no chance to make observations on cats that would show analgesic actions in headaches. But since the observable effects on cats are so nearly identical, it is anly fair to presume that the 'synthetic' and the mixture are practically alike in action."

Thus it is seen that Peralga, stripped o fthe glittering claptrap, is revealed as essentially a mixture of two well known drugs—deserving no claim of originality; in fact it contains a chemical impurity caused by decomposition of the mixture under heat. Certain it is that a mixture of barbital and amidopyrin is not a contribution to synthetic chemistry[2] as we know the term in this country.

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[2] Since this was written, an abstract of an article by J. Herzog has been published (Chem. Zentralbl., Feb. 14, 1923) where in essentially the same conclusions are reported as given above.

OWL ENAMEL TOILET CREAM

(Abstracted, with additions, from The Journal A. M. A., April 7, 1923, p. 1022)

A Poisonous Cosmetic Sold with No Warning to the Public

"Owl Enamel Toilet Cream" manufactured by the Owl Drug Co. of Kansas City, Mo., is sold for the alleged purpose of "Beautifying the Complexion and Rendering the Skin Soft and Velvety." The jar in which this preparation comes bears a label reading:

> "Think of a remedy having the power of summoning instantly to the face and neck the color and brilliancy of youth! Just what you want to use before going to the theater or shopping, as it may be applied as often as you choose during the day it gives the face instantly a soft beautiful flush and brilliancy."

Some months ago Dr. Henry W. Woltman of Rochester, Minn., sent to THE JOURNAL a report[1] of a case of lead poisoning in a woman who had been using Owl Enamel Cream. With his report Dr. Woltman sent an opened and partly used specimen of the preparation which he stated, on analysis, had showed a very high lead content. At the time Dr. Woltman's article was ready for publication in THE JOURNAL, the Propaganda department obtained from the Owl Drug Company of Kansas City some original unopened packages of Owl Enamel Cream which were examined in the Association's laboratory and the following report published in THE JOURNAL:

"An original, unopened package of Owl Enamel Toilet Cream (Pink), manufactured by the Owl Drug Co., Kansas City, Mo., was submitted to the A. M. A. Chemical Laboratory for analysis. No information was given on the label concerning the composition of the preparation. The package contained a pink, perfumed mass, having about the consistency of fresh putty. On standing the preparation became harder and apparently dried. Qualitative tests indicated the presence of a lead compound, a calcium compound, a carbonate, glycerin and traces of phosphate, iron and some substance insoluble in nitric acid which was probably talc. Bismuth salts, mercury salts, zinc salts, casein, fats, lanolin, petrolatum or starch, substances sometimes found in face creams, were absent. Analysis indicated that the composition of the preparation is essentially as follows:

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[1] Woltman, H. W.: Lead Poisoning from Face Enamel, J. A. M. A. **80**: 1685 (Nov. 11) 1922.

Lead carbonate (basic)	42.5 per cent.
Calcium carbonate	40 per cent.
Glycerin	7 per cent.
Insoluble matter (probably talc)	0.5 per cent.
Iron, phosphate and coloring	traces
Water (by difference)	10.0 per cent.

"It is evident from this analysis, therefore, that Owl Enamel Toilet Cream (Pink) is composed essentially of lead carbonate, calcium carbonate and glycerin.

Concerning the laxity of our laws in protecting the public against poisons in "patent medicines" THE JOURNAL commented as follows:

"The indiscriminate sale of a preparation of this sort is not merely a menace to the public health but a commentary on the laxity of our laws. It is notorious that certain salts of lead have for years been responsible for cases of chronic lead poisoning, due to their employment in cosmetics. As Peterson and Haines in their Text-Book of Legal Medicine and Toxicology said twenty years ago 'the use of "flake white" as a cosmetic has caused every form of chronic lead poisoning.' In spite of this any concern, responsible or irresponsible, can sell for the indiscriminate use of the girls and women of the country a cosmetic loaded down with this poisonous ingredient, and they are not required to give any hint as to the potential dangers nor even to declare the presence of the poison."

Details of Analysis

Insoluble.—A weighed portion of the material was dissolved so far as possible in warm very dilute nitric acid, the solution filtered through a weighed, Gooch crucible, the insoluble matter washed, dried, heated and weighed. From 10.0013 gm. of material an insoluble residue of 0.0524 gm. was obtained, equivalent to 0.523 per cent. A duplicate weighing 20.0162 gm. (from which the glycerin had been extracted by alcohol) gave an insoluble residue weighing 0.1157 gm. equivalent to 0.578 per cent. Average, 0.551 per cent. of insoluble matter. The filtrate from the determination of the insoluble material was diluted to 1,000 c.c. and aliquot portions used for the determinations of lead and calcium.

Lead.—An aliquot portion (100 c.c.) of the diluted filtrate from the determination of the insoluble matter was evaporated almost to dryness on the steam bath, the residue taken up in hot water and hydrogen sulphid passed in unitl all of the lead had been precipitated as sulphid. The precipitate was dissolved so far as possible in hot, very dilute nitric acid, the solution filtered, the filtrate evaporated almost to dryness in presence of an excess of sulphuric acid, the mixture diluted with water and sufficient alcohol added to make the content about 25 per cent., the mixture allowed to stand over night and the lead sulphate, collected, heated and weighed in the usual way. The lead sulphate from 100 c.c. of the solution, equivalent to 1.00013 gm. weighed 0.4953 gm., equivalent to 42.21 per cent. of basic lead carbonate, $(PbC0_3)_2+Pb(OH)_2$. A duplicate of 100 c.c. gave 0.5022 gm. of lead sulphate equivalent to 42.81 per cent. of basic lead carbonate. Average, 42.5 per cent. of basic lead carbonate. The filtrate from the lead sulphid precipitate (containing hydrogen sulphid) was evaporated to remove hydrogen sulphid and the residue used for the determination of calcium.

Calcium.—The filtrate was warmed, an excess of ammonium oxalate solution added and sufficient ammonia water to insure the mixture being alkaline. After standing over night the calcium oxalate was collected, redissolved in dilute hydrochloric acid, reprecipitated, collected, heated and weighed as calcium carbonate in the usual way. From 100 c.c. of solution, representing 1.00013 gm. of original material 0.4057 gm. of calcium carbonate was obtained, equivalent to 40.56 per cent. of calcium carbonate in the original material. A duplicate gave 0.3966 per cent. of calcium carbonate equivalent to 39.65 per cent. Average, 40.10 per cent. of calcium carbonate.

Glycerin.—The powdered material was extracted with alcohol, the mixture filtered, the filtrate evaporated on the steam bath to small volume and the evaporation continued in vacuum over sulphuric acid to constant weight. From 10.3251 gm. of material an alcoholic extract was obtained which weighed 0.7000 gm., equivalent to 6.8 per cent. A duplicate of 20.0162 gm. gave 1.3616 gm. of alcoholic extract, equivalent to 6.80 per cent. Average, 6.8 per cent. of glycerin.

EL ZAIR

Quackery's Latest Offer of an Elixir of Life

(Extracted, with additions, from The Journal A. M. A., Sept. 1, 1923, p. 768)

The student of quackery is led to wonder whether the dealer in alleged remedial agents can concoct a story too preposterous for the public to believe. The exploitation of the nostrum "El Zair" convinces one that no claims are too absurd to coax the dollars from those who seek "rejuvenation."

The El Zair advertising approach consists in (1) a typewritten letter of three pages signed "J. E. Bartlett," (*2*) a reprint of what purports to be an article by the late W. T. Stead from the English *Review of Reviews* for March, 1911, and (*3*) a "Reservation Card for Introductory El Zair Treatment." The letter from Bartlett states that there are thousands who "have personal reasons to believe that the long-sought Elixir of Youth has at last been found."

> "Older than all of these is the search for the Elixir of Youth. Have these centuries after centuries of research, thought and tireless endeavor at last enabled modern Science to discover this Elixir?"

Mr. Bartlett answers his own question by declaring that the elixir *has* been found—and is available in the form of "El Zair." The discovery of El Zair seems a matter of controversy, because the history of El Zairian quackery is not consistent. According to Bartlett, El Zair's discovery was due to the untiring investigations of "an English scientist of considerable note" one Professor James Dean Morgan, who is said to have been collaborating "with the famous Metchnikoff" at the "University of Bonn." In passing, it may be said that there seems to be no evidence that Metchnikoff ever did research work at Bonn.

> "Like Metchnikoff he was trying to pick up the lost threads dropped by the ancient alchemists and medieval philosophers."

Professor Morgan—still according to Bartlett—finally discovered his elixir and returned to England. There he "found a member of his family, Mrs. Frances Campbell, very seriously ill." He immediately sent back to Bonn for "a quantity of his new formula" with the result that Mrs. Campbell not only regained her health but her youth and, to quote the lady, "In an incredibly short space of time I had all the world crying out to me to give it to them at any price."

The Bartlett letter states further that Mr. Stead, editor of the *Review of Reviews* was so impressed with the marvelous possibilities in El Zair that he "sailed on the Titanic to offer to America the benefits of its truly astonishing results." The destruction of that ill-fated ship and the resultant death of Mr. Stead is said to have "delayed El Zair's coming to America, a delay that was further prolonged by the chaotic conditions resulting from the World War. But:

> ". . . even these tragic delays had their elements of good fortune; for during this intervening time large deposits were discovered of the ingredients which had made 'EL ZAIR' so costly. And as a result 'EL ZAIR' has come to America at a cost so moderate that anyone sincerely anxious to derive its benefits can readily afford it."

The Bartlett letter closes with the statement that the action of "El Zair" is "to withdraw from the pores and the tissues of the skin the calcareous and other waste matter which results in premature old age, and in the many diseases which are forerunners of it." El Zair is applied externally with a sponge and is "guaranteed harmless." The price of a full treatment is $6.00, but Mr. Bartlett encloses a "Reservation Card" for an "Introductory Treatment" for $2.00.

In connection with the composition it is interesting to note that after Stead's first article in the March, 1911, English *Review of Reviews* there was an editorial on El Zair in the May, 1911, issue. It was there stated that "the lady who rode over the mountains of North Africa in order to gather the mystic herbs from which the Elixir is brewed" was charging one hundred pounds sterling for the stuff. Then Mr. Stead had a final announcement in the issue of December, 1911, stating that the woman who had the wonderful herbs from which El Zair was made, wished to be known as "Mrs. Merlin." Mr. Stead stated further that, according to the Arabic manuscript in Mrs. Merlin's possession:

> "He who would use El Zair must take it internally and apply it externally with undeviating regularity. If he shrinks from the regular performance of the necessary rites let him pass by—El Zair is not for him."

It should be borne in mind, then, that the original El Zair was an infusion of herbs and was to be taken internally and used externally. These facts are interesting when compared with the present exploitation.

A "treatment" of El Zair was ordered. Before the specimen arrived there came another typewritten letter from J. E. Bartlett expressing thanks for the order, stating that the treatment was being sent and giving instructions in the use of the Elixir of Youth. The purchaser was told to dissolve the powdered El Zair in water and sponge the body daily with the solution. He was urged to squeeze out the sponge after the treatment and save the spongings in separate bottles. The letter declared that "the spongings would gradually get darker until they sometimes become almost black." This is the "deeper seated waste matter" which El Zair removes and which, according to El Zairian theories, is the cause of old age and its infirmities. With the letter there was an advertising circular whose verbiage followed closely the tenets of mail-order quackery. Part of the material is the report of an alleged "Clinical Test" said to have been "conducted by Eustace H. Gane, chemist, 1063 Sterling Place, Brooklyn." Mr. Gane's name is already familiar to readers of the Propaganda department as the author of a puff for a fake "obesity cure" put out by one R. Lincoln Graham of New York City. Possibly time will teach Mr. Gane that selling his services to quacks does not redound either to the credit of his profession or to his own reputation.

The specimen of El Zair finally arrived and was turned over to the laboratory which in due time made the following report:

LABORATORY REPORT

One original bottle of "El Zair" manufactured by "El Zair, Inc., 43 West 16th St., New York City," was submitted to the Chemical Laboratory for examination. El Zair consisted of a lumpy white substance, which was in a moist state. It had a strong, pungent odor of acetic acid; also an aromatic odor resembling oil of bergamot; when dissolved in water the acetic acid odor was not so pronounced. The product was evidently impure as some straw and dirt were easily detectable. Nonvolatile organic matter was absent. When the mixture was treated with alcohol and filtered, on evaporation the filtrate left no residue. When a specimen of the substance was dried for two hours at from 200 to 210 C., the loss in weight was 53.3 per cent. Qualitative tests indicated the absence of all heavy metals; also absence of calcium, barium and strontium; magnesium, a trace of sodium and sulphate were present. Quantitative determination yielded the following:

Acetic acid (calculated as absolute)	27.60 per cent.
Magnesium (Mg^{++})	8.41 per cent.
Sulphate (SO_4^{--})	33.92 per cent.

This is equivalent to approximately 42 per cent. of magnesium sulphate, calculated as anhydrous and 28 per cent. glacial acetic acid. (The magnesium sulphate of commerce varies much in its water of crystallization; if pure, it contains 7 molecules which weighs about twice as much as the anhydrous.) Essentially, the product may be considered to consist of 1 part glacial acetic acid to 3 parts of magnesium sulphate, U. S. P. (Epsom salt) perfumed with oil of bergamot. According to the directions, the contents of the bottle are to be added to a pint of water. An essentially similar solution can be made by dissolving 2½ ounces of Epsom salt in a pint of distilled vinegar (containing about 5 per cent. acetic acid).

In concluding its article THE JOURNAL stated:

"Here, then, we have the new Elixir of Life, handed down from the old Arabians and obtained with much toil and travail by an intrepid English woman who rode over the mountains of North Africa in order to gather its mystic ingredients—Epsom salt and vinegar. Here we have, to quote from the enterprising Mr. Bartlett, the results of 'centuries after centuries of research, thought and tireless endeavor'—Epsom salt and vinegar. Here stands the crowning achievement of the English scientist of note who, like Metchnikoff tried 'to pick up the lost threads dropped by the ancient alchemists and medieval philosophers'—Epsom salt and vinegar. Here is the marvelous combination that brought back to life a dying consumptive, that grew hair on the bald thatch of a septuagenarian, that cured a crippled American millionaire of a tuberculous knee joint, that permitted a 'noble lady who had long since given up all hope of presenting her lord with an heir' to become a 'happy mother,' that made a new man of a mentally and physically tired out distinguished novelist; that rejuvenated a 'member of a great ducal family'; that called forth paeans of praise from Lord Redesdale, the Countess of Warwick and Sir Charles Hawtrey—Epsom salt and vinegar.

"The exploiters of 'El Zair' charge $6.00 for six weeks' treatment. For those who are willing to forego the thrill of reading the El Zair literature but still wish to be rejuvenated, to grow hair on bald heads, to cure tuberculous joints, or to become happy mothers, we suggest that the same results can be obtained by purchasing half a pound of commercial Epsom salt and a quart of 'white' vinegar."

Details of Analysis

The bottle contained 91 gm. of substance. No precipitate was given by saturation with hydrogen sulphid either in acid solution containing El Zair or in a solution to which ammonium chlorid and ammonia water had been added. To a solution of El Zair, to which was added ammonium chlorid and ammonium carbonate solutions, addition of sodium phosphate solution yielded a copious precipitate (Mg^{++}). The addition of barium chlorid solution to a solution of El Zair, previously acidified with hydrochloric acid, caused a heavy precipitate ($SO_4^{=}$). Tests for carbonate, citrate, halids, tartrate were negative. Sodium flame test was weakly positive. On heating gently, there was no charring.

Loss in Weight.—4.9485 gm. of the original sample were heated in a platinum dish on a water bath for two hours, and then in an oven at from 200 to 210 C. for two hours. The loss in weight was 2.6385 gm., equivalent to 53.3 per cent. On heating the contents of the platinum dish over a flame for one-half hour, the ash weighed 1.6078, equivalent to 32 per cent.

Acetic Acid.—For the acetic acid, magnesium and sulphate determination, 4.7233 gm. of the original specimen were dissolved in 500 c.c. and aliquot portions used. The solution was titrated with standard sodium hydroxid solution, phenolphthalein being used as indicator. (*a*) 50 c.c. require 2.18 c.c. of N/1 NaOH, equivalent to 27.6 per cent. of acetic acid—CH_3COOH; (*b*) 50 c.c. required 2.18 c.c. N/1 NaOH, equivalent to 27.6 per cent. of acetic acid; (*c*) 50 c.c. required 21.65 c.c. of N/10 NaOH, equivalent to 27.5 per cent. of acetic acid.

Magnesium (Mg^{++}).—Magnesium was precipitated in the usual manner as magnesium ammonium phosphate ($Mg(NH_4)PO_4$), filtered into a weighted Gooch crucible and the precipitate converted into magnesium pyrophosphate, ($Mg_2P_4O_7$). (*a*) 100 c.c. yielded 0.3591 gm. of magnesium pyrophosphate, equivalent to 8.32 per cent. of magnesium; (*b*) 100 c.c. of the solution yielded 0.3667 gm. of magnesium pyrophosphate, equivalent to 8.48 per cent. of magnesium.

Sulphate ($SO_4^{=}$).—An aliquot portion was acidified with hydrochloric acid, heated and an excess of barium chlorid added to the hot solution. The precipitate was filtered into a tared Gooch crucible, washed well and weighed. (*a*) 50 c.c. yielded 0.3885 gm. of barium sulphate, equivalent to 33.84 per cent. of $SO_4^{=}$; (*b*) 50 c.c. yielded 0.3902 gm. of barium sulphate, equivalent to 33.98 per cent. of $SO_4^{=}$.

VAN ESS

Another Bid for Bald-Headed Optimists

(Abstracted, with additions, from The Journal A. M. A., Oct. 27, 1923, p. 1460)

The Van Ess Laboratories, Inc., of Chicago, put out "Van Ess Special Dandruff Massage" and "Van Ess Liquid Scalp Massage."

Van Sant, the first part of whose surname (Van S.) doubtless has been modified to name the products, seems, until within the last year or two, to have been connected with a San Francisco concern known as the Overseas Trading Company of California. The story goes that this concern went out of existence under somewhat sensational circumstances and with little satisfaction to the creditors.

The physical make-up of the package in which a cosmetic nostrum is dispensed has large psychological possibilities. Van Ess comes in a wide-mouthed bottle of characteristic shape. Part of the paraphernalia is a rubber stopper that has several nipples on the outer surface. Three of the nipples are hollow. After opening the bottle this nipple-surfaced rubber cap is screwed onto the neck and the optimist who expects to grow hair rubs these nipples over the scalp. An interesting and highly imaginative picture in the little booklet that comes with the nostrum shows just how each rubber nipple fits into its own particular hair follicle, removes the caked sebum and causes the poor stunted hair to flourish like the green bay tree.

Some of the claims made for Van Ess are:

"We Guarantee To Make Hair Grow. To Make It Silky, Lustrous. Beautiful."

"Remove that infected oil—Sebum—and soon your hair has the silken loveliness, the sheen and beauty for which every woman strives. Our method accomplishes that result."

> "We guarantee to stop falling hair in two weeks. We guarantee to grow new hair. If we fail, your money back without question."
>
> "Experiments of years prove it effective on 91 heads in 100. Foremost authorities approve it. World noted dermatologists now employ it —many charge as much as $500 for the treatment."

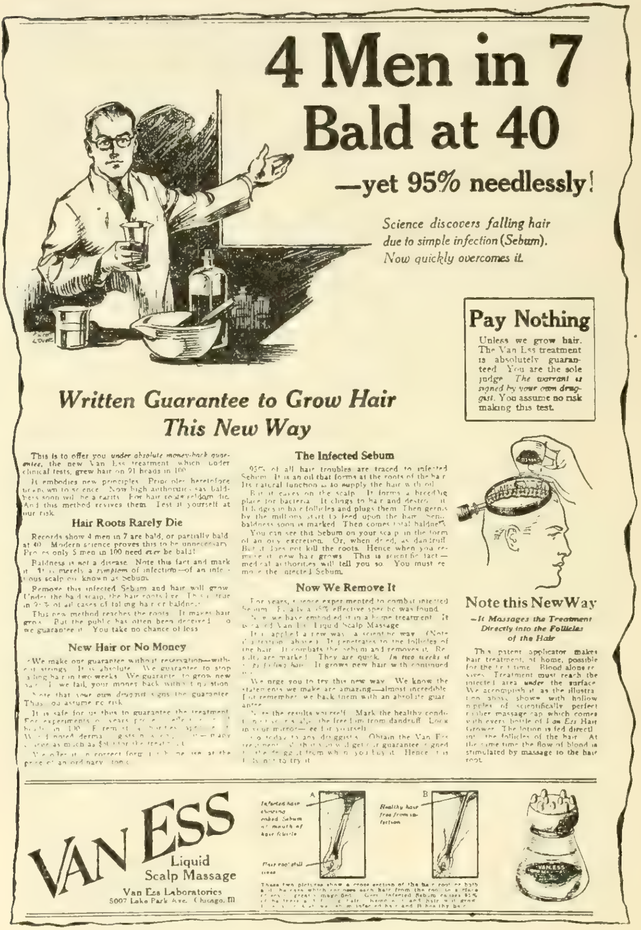
The "money back guarantee" sounds plausible and should be counted on to sell many "treatments." The bald-headed contingent will use the stuff, decide after spending varying amounts of money on it that they have been humbugged once more, charge it up to profit and loss and forget it—until the next sure-fire hair-grower comes to their attention. If, as someone who should know, has said, a sucker is born every minute, there is a bald-headed sucker born every ten minutes. This perennial group makes a sufficiently wide and lush field for the exploiters of cures for baldness. So long as hope springs eternal in the breast of the bald-headed and such cures are advertised the latter will sell and the former be "sold."

As The Journal has received many inquiries, a specimen of the Van Ess Special Drandruff Massage was purchased, analyzed and the following report published in The Journal:

"'Van Ess Special Dandruff Massage' is sold in an amber colored bottle containing about 4 fluidounces. The label declares the presence of 20 per cent. of alcohol. The preparation is a perfumed liquid which separates into two layers on standing. The upper layer, which amounts to a little more than one-third (about 36 per cent.) of the whole, is pale yellow and consists essentially of a petroleum oil which appears to be kerosene. The lower layer, which is a darker yellow, appears to be composed of water and alcohol containing small amounts of quinin sulphate, coloring matter and perfume. Although 20 per cent. of alcohol is declared on the label, analysis disclosed only about 14 per cent. The results of the examination indicate that the composition of the preparation is essentially as follows:

Kerosene	36 per cent.
Alcohol	14 per cent.
Quinin sulphate	0.06 gm. per 100 c.c.
Water, perfume and dye to make	100 c.c.

"It seems probable that a mixture of 35 parts of kerosene and 15 parts of alcohol, denatured by the addition of 2 grains of quinin sulphate per fluidounce and 50 parts of water would have whatever therapeutic properties the Van Ess Special Dandruff Massage possesses."



4 Men in 7 Bald at 40

—yet 95% needlessly!

Science discovers falling hair due to simple infection (Sebum). Now quickly overcomes it.

Pay Nothing

Unless we grow hair. The Van Ess treatment is absolutely guaranteed. You are the sole judge. *The warrant is signed by your own druggist.* You assume no risk making this test.

Written Guarantee to Grow Hair This New Way

This is to offer you *under absolute money-back guarantee,* the new Van Ess treatment which under clinical tests, grew hair on 91 heads in 100.

It embodies new principles. Principles heretofore unknown to science. Now high authorities say baldheads soon will be a rarity. For hair roots seldom die. And this method revives them. Test it yourself at our risk.

Hair Roots Rarely Die

Records show 4 men in 7 are bald, or partially bald at 40. Modern science proves this to be unnecessary. Proves only 5 men in 100 need *ever* be bald!

Baldness is not a disease. Note this fact and mark it. It is merely a *symptom* of infection—of an infectious scalp oil known as Sebum.

Remove this infected Sebum and hair will grow. Under the bald scalp, the hair roots live. This is true in [illegible] of all cases of falling hair or baldness.

This new method reaches the roots. It makes hair grow. But the public has often been deceived [illegible] we guarantee it. You take no chance of loss.

New Hair or No Money

We make our guarantee without reservation—without strings. It is absolute. We guarantee to stop falling hair in two weeks. We guarantee to grow new hair. If we fail, your money back without question.

Note that your own *druggist* signs the guarantee. Thus you assume no risk.

It is safe for us thus to guarantee the treatment. For experiments of years [illegible] heads in 100. [illegible] noted derma[illegible] as much as [illegible] for the treatment.

We offer it in correct form [illegible] at the price of an ordinary tonic.

The Infected Sebum

95% of all hair troubles are traced to infected Sebum. It is an oil that forms at the roots of the hair. Its natural function is to supply the hair with oil.

But it cakes on the scalp. It forms a breeding place for bacteria. It clings to hair and destroys it. It lodges in hair follicles and plugs them. Then germs by the millions start to feed upon the hair. Then baldness soon is marked. Then comes total baldness.

You can see this Sebum on your scalp in the form of an oily excretion. Or, when dried, as dandruff. But it does not kill the roots. Hence when you remove it new hair grows. This is scientific fact—medical authorities will tell you so. You must remove the infected Sebum.

Now We Remove It

For years, science experimented to combat infected Sebum. Finally a [illegible] effective specific was found.

Now we have embodied it in a home treatment. It is called Van Ess Liquid Scalp Massage.

It is applied a new way, a scientific way. (Note illustration above.) It penetrates to the follicles of the hair. It combats the Sebum and removes it. Results are marked. They are quick. *In two weeks it stops falling hair.* It grows new hair with continued use.

We urge you to try this new way. We know the statements we make are amazing—almost incredible. But remember we back them with an absolute guarantee.

See the results yourself. Mark the healthy condition of your scalp, the freedom from dandruff. Look in your mirror—see for yourself.

Go today to any druggist. Obtain the Van Ess treatment. [illegible] get our guarantee signed by the druggist from whom you buy it. Hence it is [illegible] to try it.

Note this New Way

—It Massages the Treatment Directly into the Follicles of the Hair

This patent applicator makes hair treatment, at home, possible for the first time. Blood alone revives. Treatment must reach the infected area **under the surface**. We accomplish it as the illustration above shows with hollow nipples of scientifically perfect rubber massage cap which comes with every bottle of *Van Ess* Hair Grower. The lotion is fed directly into the follicles of the hair. At the same time the flow of blood is stimulated by massage to the hair root.

VAN ESS
Liquid Scalp Massage
Van Ess Laboratories
5007 Lake Park Ave. Chicago, Ill

A

Infected hair showing caked Sebum at mouth of hair follicle

Hair root still lives

B

Healthy hair free from infection

These two pictures show a cross section of the hair root or bulb and the case which covers each hair from the root to surface [illegible] greatly magnified. [illegible] Infected Sebum causes 95% of [illegible] falling hair. [illegible] hair will grow. [illegible] infected hair and B healthy hair.

Greatly reduced reproduction of a typical Van Ess Advertisement. The original measured 9 inches by 13 inches. Such advertising in metropolitan papers is expensive, but the profits on Van Ess can doubtless stand it.

Concerning the preparation The Journal commented as follows:

"If, as seems probable, Van Ess Special Dandruff Massage is made with denatured alcohol, the actual cost of the ingredients should not exceed twenty cents a gallon. The market price of the preparation is $1.50 for four ounces. Even after the Van Ess concern has paid its advertising bills, and they must be heavy, there should still be a handsome profit at selling twenty cents' worth of kerosene and alcohol for forty-eight dollars. Until the accumulated experience of the bald-headed public overcomes the persuasive psychology of the advertising, Mr. Van Sant's latest venture should prove more profitable than the Overseas Trading Company of California."

Details of Analysis

Kerosene.—As purchased, Van Ess Special Dandruff Massage occurs in two layers. The contents of a package were measured. The total volume measured 117 c.c., or nearly 4 fluidounces. As completely as possible, the material was poured into a separator and the lower layer drawn off and measured. The volume of the material removed measured 75 c.c. or about 64 per cent. of the total. The material remaining in the separator was washed with water twice and the washings added to the material (lower layer) previously removed. The material in the separator was filtered through dry filter paper. The specific gravity at $\frac{15.6 \text{ C.}}{15.6 \text{ C.}}$ was 0.84183. This material burned with a smoky flame when ignited and possessed a strong odor like kerosene.

Total Alkaloids.—The aqueous material first removed from the separator was evaporated on the water bath to decrease its volume to about 50 c.c., an excess of ammonia water added to the cooled solution and the mixture shaken three times with 10 c.c. portions of chloroform. The solvent was washed with water, allowed to evaporate spontaneously and the residue dried at 100 C. and weighed. The residue from 117 c.c. of original material weighed 0.0534 gm., equivalent to 0.0614 gm. of quinin sulphate, U. S. P., per 100 c.c. The residue gave the usual tests for quinin.

Alcohol.—Alcohol was determined by shaking the mixture thoroughly to insure a uniform sample, measuring 100 c.c. at 15 C., distilling and determining the alcohol in the distillate according to the tentative method of the Association of

Official Agricultural Chemists. (Methods of Analysis, Association of Official Agricultural Chemists, 1919, p. 204.) The specific gravity of the final distillate at $\frac{15.6\ C}{15.6\ C}$ was 0.98201, equivalent to 14.17 per cent. of absolute alcohol.

MONEY IN MUD

(Abstracted, with additions, from Hygeia, November, 1923, p. 504)

During the last year or two the cosmetic market has been glutted with a veritable avalanche of so-called complexion clays and face packs.

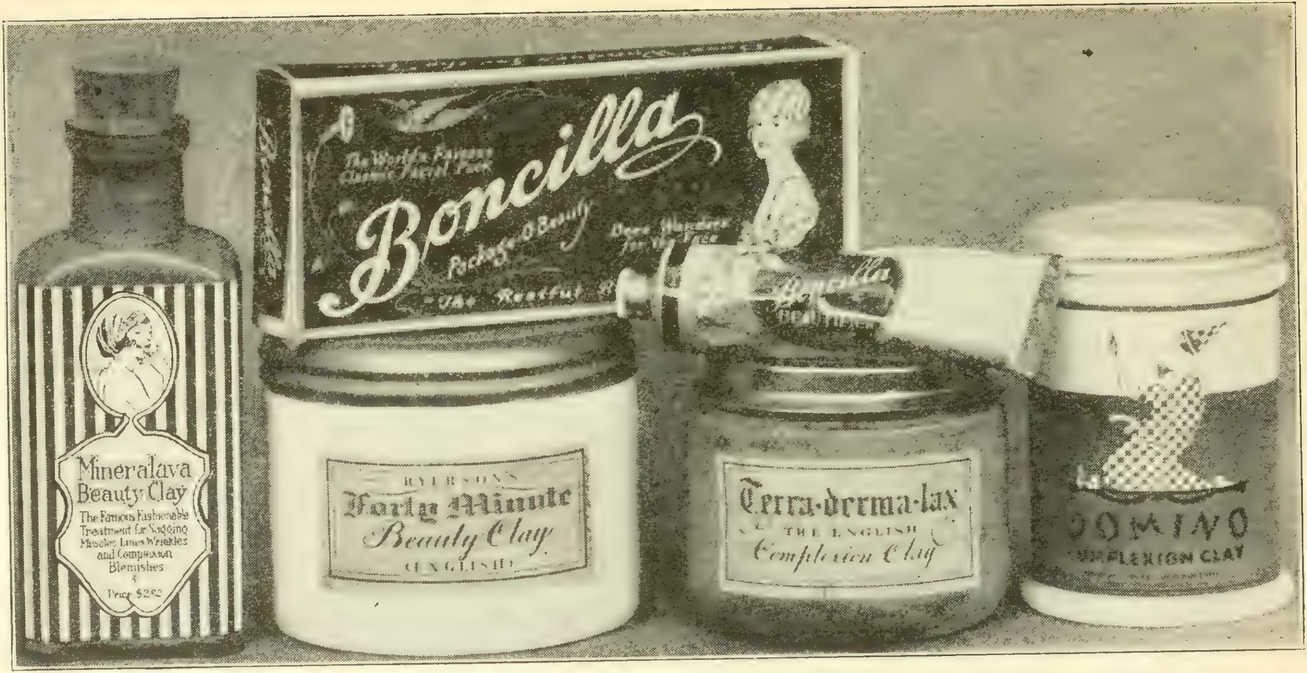
Terra-derma-lax

One of the most blatantly advertised of the complexion clays is "Terra-derma-lax." This preparation, a small jar of which sells for $2.50, is alleged to be the "remarkable discovery of a young English scientist," one M. J. McGowan, whose picture adorns most of the advertising. According to the advertisements, McGowan, while only thirty-one years old, has had "ten years' experience as a dermatologist." Investigation has failed to show that Mr. McGowan ever had even ten minutes' experience as a dermatologist or that he had ever made a single contribution to scientific literature. Inquiries have elicited the information that this "scientist" worked in a subordinate capacity in the soap and fertilizer departments in the Chicago stockyards. Terra-derma-lax is sold by the Dermatological Laboratories of Chicago.

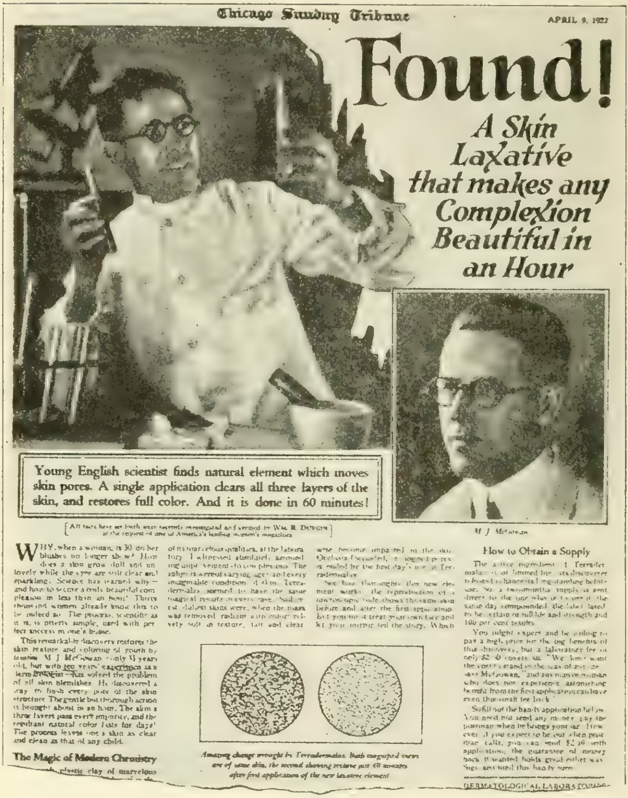
In its first stages the Terra-derma-lax business was a mail-order one. The public was told that "Terra-derma-lax cannot be stocked by druggists" as the "active ingredient that loosens the pores of the skin structure must be fresh." The clay wouldn't keep! Later it was decided, apparently, that the product would stay fresh long enough for the retail druggist to assume some of the financial responsibility for handling it. Then feminine seekers after beauty were told: "Stop at your dealer's today and ask for Terra-derma-lax."

Boncilla Beautifier

According to the advertising the "Original, Genuine, Clasmic Facial Pack" is "Boncilla Beautifier"—$1.00 for a two ounce tube. With it, "you don't have to wait weeks and



Why "beauty specialists" get rich. A few cents' worth of clay in a fancy jar, bottle or tube; colored labels and more highly colored claims and the public will pay from one to five dollars for a package



Chicago Sunday Tribune

APRIL 9, 1922

Found!

A Skin Laxative that makes any Complexion Beautiful in an Hour

Young English scientist finds natural element which moves skin pores. A single application clears all three layers of the skin, and restores full color. And it is done in 60 minutes!

The Magic of Modern Chemistry

How to Obtain a Supply

No, this is not Harold Lloyd in "Safety Last" nor Ed. Wynn in "The Perfect Fool." It is Mr. M. J. McGowan posing as a scientist for the purpose of selling "Terra-derma-lax." The advertisement claims that Mr. McGowan has had "ten years' experience as a dermatologist;" investigation has failed to show that the gentleman ever had ten minutes' experience as a dermatologist.

months to see results"; you spread the stuff on your face, allow it to dry, and when you remove it find a "youthful complexion, beauty that is natural, lasting, real." Boncilla Beautifier is sold by the Boncilla Laboratories of Indianapolis.

Domino Complexion Clay

"I could hardly believe my eyes. Just thirty minutes before my face had been blemished and unsightly; my skin had been coarse, sallow and lifeless. Now it was actually transformed. I was amazed when I saw how beautiful my complexion had become—how soft its texture, how exquisite its coloring."

Thus, the opening blurb from a full-page advertisment of "Domino Complexion Clay." The advertisement is one of those heart-to-heart, personal, and confidential affairs so much affected by the exploiters of cosmetics. Domino Complexion Clay is sold by Domino House of Philadelphia.

Mineralava

"Mineralava," price $2.00 a bottle, is "Nature's Beauty Clay"; and its use is "Nature's Way to Beauty." The manufacturer admits it. Needless to say, it had a wonderful origin. It was the result, we are told, of "twenty-three years of scientific research and experiment" on the part of one Mrs. M. G. Scott. For some unknown reason Mrs. Scott is not a scientist, but a "fashionable specialist." Mineralava Beauty Clay is sold by Scott's Preparations, Inc., of New York.

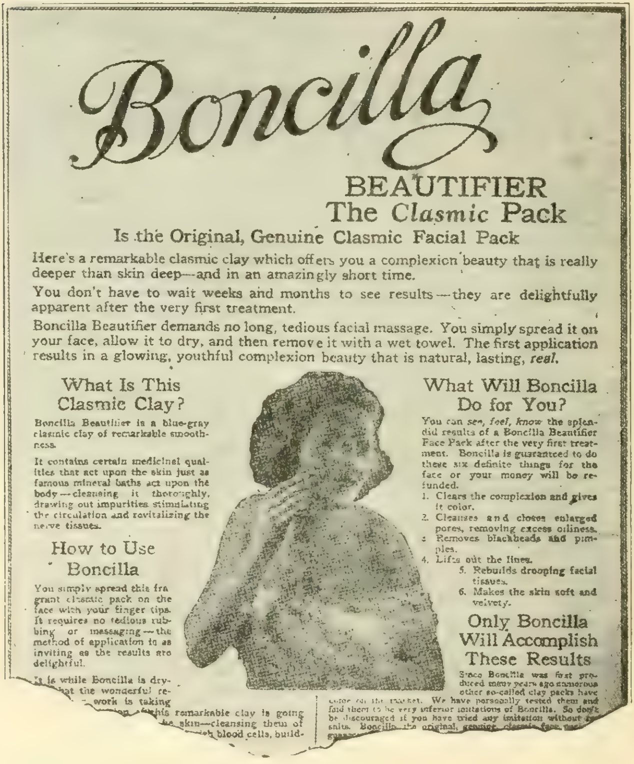
Ryerson's Forty Minute Beauty Clay

According to the label on the jar, the "Forty Minute Beauty Clay" is an English product; according to the newspaper advertisements, it is a Welsh product. Price, $5.00.

What the Chemists Found

Women seeking short cuts to beauty, having read the complexion clay advertisements, have asked: What are these products for which such marvelous results are claimed? To answer the question the Chemical Laboratory of the American Medical Association analyzed some of the market products. The five widely advertised nostrums above mentioned were purchased and the following report published:

"The products examined were: (1) 'Terra-derma-lax,' (2) 'Boncilla,' (3) 'Domino Complexion Clay,' (4) Mineralava,' and (5) 'Ryerson's Forty Minute Beauty Clay.'



Boncilla

BEAUTIFIER
The *Clasmic* Pack

Is the Original, Genuine Clasmic Facial Pack

Here's a remarkable clasmic clay which offers you a complexion beauty that is really deeper than skin deep—and in an amazingly short time.

You don't have to wait weeks and months to see results—they are delightfully apparent after the very first treatment.

Boncilla Beautifier demands no long, tedious facial massage. You simply spread it on your face, allow it to dry, and then remove it with a wet towel. The first application results in a glowing, youthful complexion beauty that is natural, lasting, *real*.

What Is This Clasmic Clay?

Boncilla Beautifier is a blue-gray clasmic clay of remarkable smoothness.

It contains certain medicinal qualities that act upon the skin just as famous mineral baths act upon the body—cleansing it thoroughly, drawing out impurities stimulating the circulation and revitalizing the nerve tissues.

How to Use Boncilla

You simply spread this fragrant clasmic pack on the face with your finger tips. It requires no tedious rubbing or massaging—the method of application is as inviting as the results are delightful.

It is while Boncilla is dry-
at the wonderful re-
work is taking
this remarkable clay is going
the skin—cleansing them of
blood cells, build-

What Will Boncilla Do for You?

You can *see*, *feel*, *know* the splendid results of a Boncilla Beautifier Face Pack after the very first treatment. Boncilla is guaranteed to do these six definite things for the face or your money will be refunded.

1. Clears the complexion and gives it color.
2. Cleanses and closes enlarged pores, removing excess oiliness.
3. Removes blackheads and pimples.
4. Lifts out the lines.
5. Rebuilds drooping facial tissues.
6. Makes the skin soft and velvety.

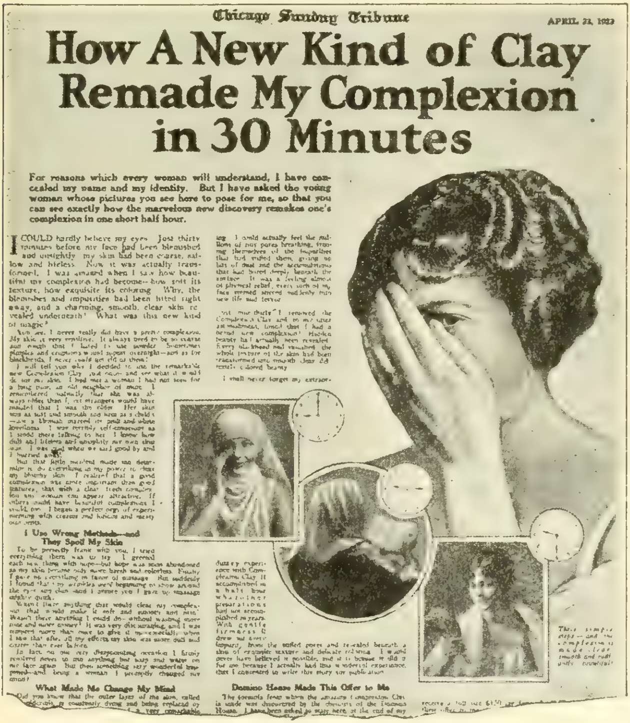
Only Boncilla Will Accomplish These Results

Since Boncilla was first produced many years ago numerous other so-called clay packs have come on the market. We have personally tested them and found them to be very inferior imitations of Boncilla. So don't be discouraged if you have tried any imitation without results. Boncilla, the original, genuine

The "Boncilla" brand of clay, if one believes the advertisement, produces a beauty that is more than skin deep.

"Boncilla Beautifier comes in a collapsible tube like toothpaste. Terra-derma-lax, Domino Complexion Clay and Ryerson's Forty Minute Beauty Clay are marketed in ointment jars. Mineralava Beauty Clay is sold in a wide-mouthed bottle accompanied by a brush with which to spread the contents on the face.

"No information concerning the composition of the several products was given on their labels except such as is contained in their names. The presence of clay in all except the (Boncilla Beautifier) is admitted by the manufacturer. Each of the products was a bluish mass of about the consistency of soft putty. Each resembled a mixture of clay and water. Some of the specimens were softer than others and contained more water.



Chicago Sunday Tribune APRIL 22, 1923

How A New Kind of Clay Remade My Complexion in 30 Minutes

For reasons which every woman will understand, I have concealed my name and my identity. But I have asked the young woman whose pictures you see here to pose for me, so that you can see exactly how the marvelous new discovery remakes one's complexion in one short half hour.

I COULD hardly believe my eyes. Just thirty minutes before my face had been blemished and unsightly, my skin had been coarse, sallow and lifeless. Now it was actually transformed. I was amazed when I saw how beautiful my complexion had become—how soft its texture, how exquisite its coloring. Why, the blemishes and impurities had been lifted right away, and a charming, smooth, clear skin revealed underneath! What was this new kind of magic?

I Use Wrong Methods—and They Spoil My Skin

What Made Me Change My Mind

Domino House Made This Offer to Me

Here we have an advertisement of "Domino Complexion Clay" which is said to make brand new complexions in thirty minutes.

"While the preparations were being studied, there were various rumors current among chemists concerning their composition.* With one exception, no substance other than clay, water, and perfume was found.

"Water was determined by drying a portion of the material at 100 C. The proportions of moisture in the several specimens varied considerably, as shown in the tabulated findings.

	Per Cent. Water
"Terra-derma-lax	62.7
"Boncilla Beautifier	48.0
"Domino Complexion Clay	38.5
"Mineralava Beauty Clay	50.8
"Ryerson's Forty Minute Beauty Clay	61.4

"One specimen, Domino Complexion Clay, contained about 5 per cent. of glycerin and about 0.2 per cent. of a salicylate, probably sodium salicylate. Most of the specimens contained considerable quantities of calcium carbonate (chalk) and small quantities each of phosphate and sulphate. These are constituents of some crude clays and their presence indicates that the clays used are evidently not high-grade products nor are they carefully purified before being used.

"From the analysis it is concluded that Terra-derma-lax, Boncilla Beautifier, Domino Complexion Clay, Mineralava Beauty Clay and Ryerson's Forty Minute Beauty Clay are essentially mixtures of clay and water."

Concerning the beauty clays and the methods used in their exploitation Dr. Cramp wrote in *Hygeia* as follows:

"Great is the power of words and wonderful the potentialities of modern advertising. Who would have believed that so prosaic a product as clay could be endowed with such esoteric qualities? A study of the 'patent medicine' business convinces one that with the right kind of advertising 'copy' and a large advertising appropriation one could become rich by selling pink dish-water as a curative agent.

"Here is a helpful hint for those women who think the path to beauty lies through the clay route: Go to your neighborhood druggist and purchase a pound of kaolin (dried, powdered clay). It will cost about twenty cents. Mix it with the same weight of water. You will then have two pounds of beauty clay equal in beautifying power to, and purer than, any of the products on the market that are sold for from $2.00 to $10.00 a pound. The only thing you will lack is the mental uplift produced by reading the ineffable bosh published by the complexion clay exploiters.

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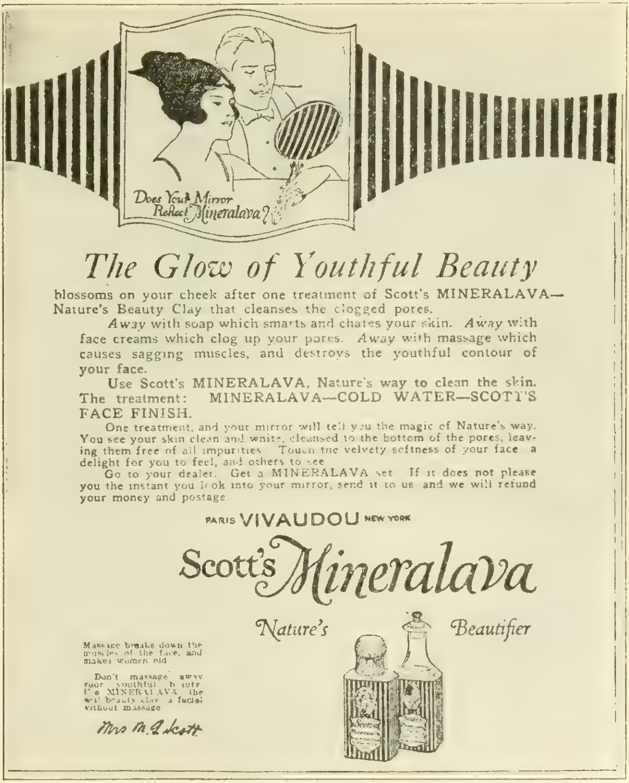
* In addition to clay and water the beauty clays were said to contain one or more of the following substances: glycerin, tragacanth jelly, mucilage of acacia, hydrogen peroxid, alum, citric acid, phenol, camphor, tincture of benzoin, saturated aqueous solution of magnesium sulphate and saturated aqueous solution of sodium borate.


Does Your Mirror
Reflect Mineralava?

The Glow of Youthful Beauty

blossoms on your cheek after one treatment of Scott's MINERALAVA—Nature's Beauty Clay that cleanses the clogged pores.

Away with soap which smarts and chafes your skin. *Away* with face creams which clog up your pores. *Away* with massage which causes sagging muscles, and destroys the youthful contour of your face.

Use Scott's MINERALAVA, Nature's way to clean the skin. The treatment: MINERALAVA—COLD WATER—SCOTT'S FACE FINISH.

One treatment, and your mirror will tell you the magic of Nature's way. You see your skin clean and white, cleansed to the bottom of the pores, leaving them free of all impurities. Touch the velvety softness of your face a delight for you to feel, and others to see.

Go to your dealer. Get a MINERALAVA set. If it does not please you the instant you look into your mirror, send it to us and we will refund your money and postage.

PARIS **VIVAUDOU** NEW YORK

Scott's *Mineralava*

Nature's Beautifier

Massage breaks down the muscles of the face, and makes women old.

Don't massage away your youthful beauty. Use MINERALAVA, the real beauty clay, a facial without massage.

Mrs M. A. Scott

"Minerlava" is said to "draw forth gently and naturally" dust, grease and the other impurities that "modern life jams deep down into the skin." A dermatologic corkscrew, as it were. And all in twelve minutes! The speed demon of complexion clays.

"Centuries ago a wise man wrote: 'The getting of treasures by a lying tongue is a vanity.' Today 'the getting of treasures by a lying tongue' is an advertising art."

Details of Analysis

At the time the beauty clays were being exploited, many rumors were current among chemists and pharmacists concerning the composition of the substances. In addition to clay, one or more of such substances as starch paste, tragacanth, mucilage of acacia, glycerin, sodium borate (borax), citric acid, phenol, camphor, tincture of benzoin, saturated solution of magnesium sulphate and hydrogen peroxid were claimed to be present.

Starch Paste.—Some of the material was boiled with water and the mixture filtered through cotton. A few drops of iodin solution were added to the cooled filtrate. No blue color resulted in any of the preparations examined.

Tragacanth Jelly.—Some of the material was boiled for several hours with dilute hydrochloric acid, the mixture allowed to stand and the supernatant liquid decanted through a filter. A portion of the neutralized filtrate did not reduce Fehling's solution on boiling.

Acacia.—This test was identical with that for tragacanth. The result was negative for each of the preparations tested.

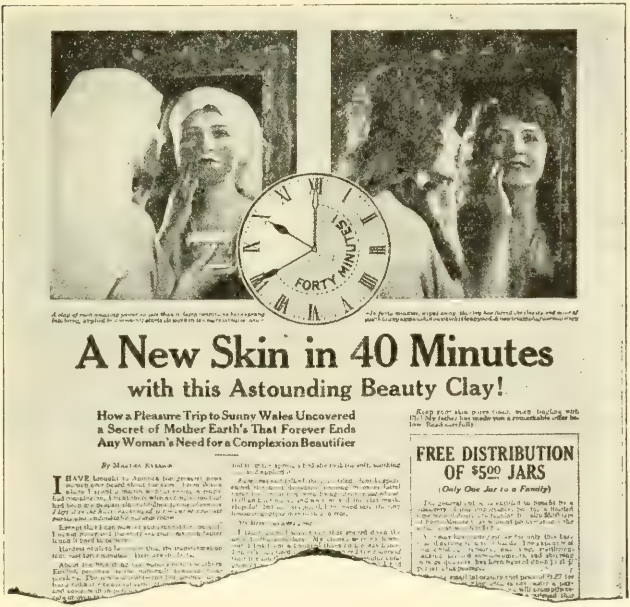
Sodium Borate (Borax).—Some of the material was shaken with water, the mixture allowed to settle and the supernatant liquid decanted through a filter. The filtrates from the several preparations were neutral or very slightly acid to litmus, thus demonstrating the absence of sodium borate.

Magnesium Sulphate.—Some of the material was triturated with water, the mixture allowed to settle and the supernatant liquid decanted through a filter. The filtrate did not respond to the usual tests for magnesium and gave evidence of only traces of sulphates. These tests were taken to indicate the absence of saturated solutions of magnesium sulphate.

Citric Acid.—Some of the filtrate, such as was used in the tests for magnesium, was tested by Denige's test for citric acid (Rep. Lab. A. M. A., Vol. 9, p. 55, 1916). The tests were negative in each case.

Phenol.—Some of the filtrate, such as was used in the test for magnesium, was treated with a few drops of ferric chlorid solution. No violet color was produced except in the case of

Domino Complexion Clay, thus demonstrating (with the one exception) the absence of phenol from each of the preparations. The absence of phenol in Domino Complexion Clay was demonstrated by the absence of a phenol-like odor after the spontaneous evaporation of an alcoholic extract of the preparation.


FORTY MINUTES

A New Skin in 40 Minutes

with this Astounding Beauty Clay!

How a Pleasure Trip to Sunny Wales Uncovered a Secret of Mother Earth's That Forever Ends Any Woman's Need for a Complexion Beautifier

FREE DISTRIBUTION OF $5.00 JARS

(Only One Jar to a Family)

"Ryerson's Forty Minute Beauty Clay" seems to be another name for McGowan's "Terra-derma-lax." They come from the same source. The illustration in the advertisement reproduced has also been used in some of the "Terra-derma-lax" advertising.

Salicylic Acid.—The only preparation, the aqueous extract of which gave a violet color with ferric chlorid, was Domino Complexion Clay. Qualitative tests indicated the presence of a combined salicylate. To determine this approximately 10 gm. were weighed, the material triturated with water and the mixture made up to a volume of 1,000 c.c. with water. After settling, a portion of the supernatant liquid was decanted through a dry, asbestos filter, 250 c.c. of the filtrate acidified with hydrochloric acid, the solution shaken successively with 3 portions of 20 c.c. of ether, the solvent allowed to evaporate spontaneously, the residue dried over sulphuric acid and weighed as salicylic acid. A portion of the filtrate representing 2.6187 gm. of original material gave 0.0041 gm. of salicylic acid, equivalent to 0.16 per cent. of salicylic acid or 0.18 per cent. of sodium salicylate.

Glycerin.—A portion of the filtrate, obtained as under salicylic acid (250 c.c.), was evaporated to about 10 c.c., the residue taken up so far as possible in 50 c.c. of alcohol, the mixture filtered, the filtrate evaporated to about 10 c.c., and an equal volume of ether added with stirring. The mixture was allowed to stand over night, filtered through a dry filter, the filter and residue washed with a mixture of equal volumes of alcohol and ether, the filtrate evaporated on a slowly simmering water bath, the residue dried over sulphuric acid and weighed. The residue was then burned and the ash subtracted from the original weight. The loss was considered as glycerin. From 250 c.c. of the filtrate, representing 2.6187 gm. of original material, a weight of 0.1186 gm. of crude glycerin was obtained and the ash from this weighed 0.0026 gm. The loss amounted to 0.1160 gm. equivalent to 4.43 per cent. of glycerin.

Camphor.—No odor suggestive of camphor was obtained from the alcoholic extracts of any of the preparations.

SLENDAFORM

"Fooling the Fat"

(Extracted, with additions, from article by A. J. Cramp, M.D., in Hygeia, Dec., 1923)

In discussing "How 'Slendaform' reduces the pocketbook," Dr. Cramp stated:

One of the latest alleged cured for obesity whose advertising appeal runs true to type is a product with the alluring name "Slendaform."

Here are some of the modest claims made for Slendaform:

"Slendaform Reduces Without Dieting, Without Exercising, Without Drugs, Without Internal Remedies."

"Just Gently Pat or Rub It in."

"And You Can Watch Yourself Grow Thin."

"Reduces any Desired Part of the Body."

"It has proven Infallible."

"Was achieved after years of constant experiment and research by a noted Obesity Specialist now practicing in New York City and who had been using it in private work for the past sixteen years with results in every case."

"The secret properties of Slendaform causes an immediate and beneficial change in the fat cells, redistributing the oily part of the fat and releasing the water which is carried away through natural channels of circulation."

"Slendaform reduces by oxidizing abnormal tissues. It actually Melts Away the Fat."

The laboratory was asked to report on the substance. The following is the analysis:

LABORATORY REPORT

One package of Slendaform was submitted to the chemical laboratory for examination. The glass jar (capacity eight ounces) contained an imperfect emulsion; after remaining unagitated for some hours, a supernatant yellow stratum appeared. The odor was that of oil of turpentine, perfume and acetic acid. The following quantitative data were obtained:

Ash	0.3 per cent.
Residue (mostly casein)	10.6 per cent.
Oil of turpentine	44.0 per cent.
Saponifiable oil	0.05 per cent.
Acetic acid (calculated as absolute)	3.0 per cent.
Water (by difference)	42.4 per cent.

According to the analysis, the produce is a liniment consisting of essentially 10 parts of casein (used as an emulsifying agent) mixed with approximately 50 parts (by volume) of oil of turpentine, 10 parts of acetic acid, U. S. P. (36 per cent.), and 30 parts of water, containing added perfume and coloring. The small amount of saponifiable oil present is probably an impurity (fat) in the casein.

As was stated by Dr. Cramp "it should not be necessary, although probably it is necessary, to say that there is no substance known which, applied to the surface of the body, will reduce the weight. . . . Those who wish to produce a mixture essentially similar to Slendaform can do so by purchasing one-fourth pint each of oil of turpentine and commercial vinegar and mixing. While this will not form an emulsion the mixture can be shaken just before using. At an expenditure of a few cents, one can get an amount of material equal to that of a $5 jar of Slendaform and every whit as efficacious in reducing weight."

Details of Analysis

Qualitative Tests.—Besides the odor of oil of turpentine and acetic acid, the product had the following characteristics: A white substance was present which was thrown out by the addition of alcohol so that it could be removed by filtration. This latter substance gave the usual protein reactions and was soluble in alkali hydroxid or sodium oxalate solutions. It was concluded that the substance was largely, if not entirely, commercial casein. When some of the original material was heated in a small, dry distillation flask, the distillate was in two layers, showing the presence of water as well as oil of turpentine. On heating the aqueous fraction with alcohol and sulphuric acid, the characteristic odor of ethyl acetate was detected.

Quantitative Determinations.—A weighed sample of the original specimen (the contents having been well shaken before taking sample) was placed in an apparatus for steam distillation. The oil of turpentine and the acetic acid were carried over by the steam and the distillate collected until 100 c.c. had come over (the liquid remaining in the distllation apparatus was treated with phenolphthalein and a drop of N/10 sodium hydroxid solution; the red color imparted showed the absence of acid). (a) 22.2029 gm. yielded 11.2 c.c., which calculated as turpentine (specific gravity 0.87) is equivalent to 9.75 gm. or 43.9 per cent. by weight. The clear solution was carefully drawn off through a separatory funnel and titrated with N/10 sodium hydroxid solution. The amount required was 11.0 c.c. equivalent to 2.9 per cent. of acetic acid (CH_3COOH). (b) 20.3400 gm. yielded 10.35 c.c. equivalent to 9.0 gm. of oil of turpentine or 44.2 per cent. The amount required 10.2 c.c. of N/10 sodium hydroxid solution to neutralize the aqueous layer, equivalent to 3.0 per cent. of acetic acid.

Residue.—8.2850 gm. of the original specimen were transferred to a platinum evaporating dish and placed in a steam bath for 10 hours. The residue weighed 0.8925 gm., equivalent to 10.6 per cent.; the residue was ignited to constant weight; it weighed 0.0339 gm., equivalent to 0.3 per cent. ash.

Gum and Fat.—The mixture remaining in the distillation apparatus after the steam distillate "b" was filtered and washed with several portions of water. The filtrate on evaporation left practically no residue (absence of gum). The residue on the filter was treated with ten 10 c.c. portions of hot alcohol and the alcoholic washings evaporated to dryness. The residue from the alcohol treatment weighted 0.0106 gm. (0.05 per cent.) and resembled rancid butter.

GLY-SO-IODONATE

Extracted, with additions, from The Journal A. M. A., Dec. 22, 1923,, p. 2123

In July, 1921, Charles E. Huchings requested consideration by the Council on Pharmacy and Chemistry of Gly-So-Iodonate. The product, said to be a "chemical germicide-antiseptic," was "owned and controlled exclusively by the Wisconsin Medical Laboratory" which is at the present time claimed to be affiliated with the National Medical Research Laboratories, Milwaukee, Wis.

The composition of Gly-So-Iodonate was originally stated to be:

	Per Cent.
"Double distilled water	81
Alcohol	10
Glycerin	2
Solids	7

Percentage of solids as follows:

Sodium Carbonate	2.50
Sodium Chlorid	1.60
Sodium Sulphate	0.65
Sodium Bicarbonate	0.40
Potassium Carbonate	0.15
Alumina Oxid	0.05
Calcium Sulphate	0.10
Magnesium	0.05
Boracic Acid	0.30
Potassium Iodid	0.30
Iodin	0.40
Corrosive Sublimate	0.50"

The method of preparation was given as follows:

"Composition and chemicals used in the preparation of Gly-so-iodonate; First Part:

Sodium Carbonate	36.00
Sodium Chlorid	23.00
Sodium Sulphate	10.06
Sodium Bicarbonate	6.02
Potassium Carbonate	2.18
Alumina Oxid	1.50
Calcium Sulphate	2.72
Magnesium Sulphate	1.52
Boracic Acid	5.00
Potassium Iodid	5.00
Iodin	7.00

"The method of completing the solution is as follows, Second Part:

> 3,219 c.c. of double distilled water is brought to a boiling point of 225 degrees (F). After boiling for a period, 20 grains of corrosive sublimate is added—solution is again held at boiling point, then the fused chemicals (part one) is added—boiling is again held for a period, after which the whole is submitted to a special process of distillation. After cooling to a certain degree determined by years of trials, 450 c.c. of 190° alcohol is added—again distilled, and the 115 c.c. of C. P. glycerin is added—final process is another special distillation for bottling."

"The above quantities are used for making one gallon."

The Council considered the information, and the following points were presented to the Wisconsin Medical Laboratory:

I. *Composition Not Correctly Declared.*—Obviously the formula presented was an impossible one: (1) any free iodin added in accordance with the formula would react with the alkali carbonate to yield alkali iodid and alkali iodate, and (2) mercuric chlorid would react with alkali iodids to give an alkali mercuric iodid. Gly-So-Iodonate, moreover, was referred to as a distillate, for in the process of manufacture, as submitted, the solids of the formula were dissolved in water, the solution distilled and the glycerin and alcohol added to the distillate. It was safe to predict that, no matter what the interactions of the ingredients may have been, the salts of sodium, potassium, magnesium, calcium, etc., would not be sufficiently volatile to permit their distillation with the water vapors.

II. *Formula Needlessly Complex and Irrational.*—The finished Gly-So-Iodonate, a "non-poisonous" "distillate," according to the submission of the manufacturer, was a product "presenting and maintaining a dual duty of germicide and healer." It was said not to be deteriorated by "light waves, sun rays, heat and cold" and it was claimed, furthermore, that "the various chemicals are so arranged to either [sic] take up all tissue fluids and hold them in suspension, against growth, or dry up unessential exudates," "each [chemical] fulfilling a specific action within the exudates and sebums common with most wounds." In the end no evidence was submitted to demonstrate the superiority of the mixture over that of a solution of the well-known potassium mercuric iodid of equivalent concentration.

III. *Label Not Acceptable and Name Not Descriptive.*—The amount of poisonous material, mercury compound (potassium mercuric iodid?) in a given quantity was not declared on the label and the name Gly-So-Iodonate is not descriptive of the potent ingredient of the mixture.

The manufacturing company made a reply to this report, but the reply contained no statement of facts which altered the conflicts of Gly-So-Iodonate with the rules which govern the acceptance of products for inclusion in New and Nonofficial Remedies.

RECENT DEVELOPMENTS

From recent developments, according to the Council, it is evident than an active selling campaign for Gly-So-Iodonate is being directed toward factories and large commercial concerns by the National Medical Research Laboratories. The original Gly-So-Iodonate, with its statement of composition but slightly changed, is now claimed to be the base of three additional products supplied by the same firm—"Iomer-Mensal for nose and throat work, Saline-Merammo for genito-urinary work, and Gly-So-Dental for dentistry and mouth wash."

GLY-SO-IODONATE

Volume

	Per Cent.
Distilled Water	79
Alcohol	10
Glycerin	4
Minerals, Alkaloids, etc.	7

Per Cent. of Minerals, Alkaloids, Etc.

Corrosive Sublimate	0.75
Iodin	0.55
Chlorids	2.10
Vegetable Alkaloids	2.05
Platinum	0.45
Potassium Salts	1.10

In reference to the last mentioned products, a notice appears on the present-day label of Gly-So-Iodonate, which reads, "CAUTION-G. S. I. is especially prepared for surgical work and for all infections other than found in Ear, Nose and Throat or Genito-Urinary tract. Our various fluids are not interchangeable."

Specimens of Gly-So-Iodonate and the allied products were recently obtained in the open market, and the statements of composition of these are herewith reprinted from the labels. A glance suffices to show the incomplete and meaningless statements of composition. A comparison of the claimed composition of the products shows them to be complex mixtures varying slightly in the amount of this or that and with new ingredients added at will. The three new products have the potassium salts, stated to be in Gly-So-Iodonate, omitted; all show an increase over Gly-So-Iodonate in chlorid content and iodin (a claimed iodin increase of 2.55 per cent. in the case of Saline-Merammo). A few new ingredients are declared, such as small amounts of sodium and ammonia in Saline-Merammo, sodium and magnesium in Iomer-Mensal, and sulphids in Gly-So-Dental. All four products have one property in common: On opening a bottle, there is a distinct odor of iodoform, evidently due to the interaction of iodin and alcohol in alkaline solution.

IOMER-MENSAL	
Volume	Per Cent.
Distilled Water	74.50
Alcohol	11.50
Glycerin	4.50
Minerals, Alkaloids, etc.	9.50
Per Cent. of Minerals, Alkaloids, etc.	
Corrosive Sublimate	0.30
Iodin	1.05
Vegetable Alkaloids	2.15
Platinum	0.10
Chlorids	3.70
Sodium	1.25
Magnesium	0.75

SALINE-MERAMMO	
Volume	Per Cent.
Distilled Water	73
Alcohol	11
Glycerin	4
Minerals, Alkaloids, etc.	12
Per Cent. of Minerals, Alkaloids, etc.	
Corrosive Sublimate	0.81
Iodin	3.10
Sodium	0.74
Ammonia	0.30
Vegetable Alkaloids	2.15
Chlorids	4.50
Platinum	0.40

GLY-SO-DENTAL	
Volume	Per Cent.
Distilled Water	76
Alcohol	9.50
Glycerin	5.50
Minerals, Alkaloids, etc.	9
Per Cent. of Minerals, Alkaloids, etc.	
Corrosive Sublimate	0.60
Iodin	0.75
Chlorids	4.80
Vegetable Alkaloids	1.50
Platinum	0.25
Sulphids	1.10

Gly-So-Iodonate, the so-called base of the other preparations as now marketed, is claimed to differ from that formerly sold in that (1) in the new product there is an alleged increase of both mercuric chlorid and iodin; (2) unnamed chlorids and unnamed potassium salts are now claimed instead of the defined sodium and potassium salts, alumina oxid, etc.; (3) platinum is claimed as a new ingredient of the product, and (4) contrary to known principles of compatibility, vegetable alkaloids are claimed as new ingredients.

No statement is made as to why platinum, which has found no use in medicine, is desirable, or as to why it is claimed to be present in a quantity of nearly one half of one per cent. Obviously, there could hardly be present the alleged 0.45 per cent. either of platinum or of a salt of platinum, for this amount in one quart alone would be worth at the present market price over fifteen dollars, a sum between three and four times as great as that asked for Gly-So-Iodonate itself.

In view of the improbability of these claims, the Chemical Laboratory made the following determinations on Gly-So-Iodonate:

	Per Cent. By Weight
Vegetable alkaloids	0.001
Mercury	0.026
Mercury (0.026%) Calculated as Mercuric Chlorid (Corrosive Sublimate)	0.036
Platinum less than	0.01

The above analysis confirmed the suspicion that there were no alkaloids present; mercury was present in less than one-twentieth of the claimed amount, and platinum was present in less than one forty-fifth of the asserted amount!

In concluding its report, the Council stated:

"The original objection that the name of the product is not suggestive of the most potent ingredient still holds. The analysis made in the laboratory showed that there was no free iodin, but combined iodin, in the form of iodid and iodate. A commonly used method for the extemporaneous preparation of potassium mercuric iodid is to mix mercuric chlorid with potassium iodid. In view of this, and in consideration both of the statements made on the new and the old labels, and the findings of the association's laboratory, it is evident that the mercury contained in Gly-So-Iodonate is present in form of a complex salt such as potassium mercuric iodid and not as "corrosive sublimate" as declared. No complex compound of mercury is mentioned in the statement of composition; instead the asserted presence of free iodin is stressed, and the name itself is suggestive of iodin rather than mercury.

"In the advertising that is being sent to commercial concerns, the National Medical Research Laboratories make many claims for the superiority of Gly-So-Iodonate and its allied products:

> G-S-I is, we feel, the BACTERICIDE the medical world has searched for since the days of LISTER.
>
> Indicated in every case which formerly called for Iodine, Phenol, Silver Nitrate, or Caustics.
>
> G-S-I is a bactericide of enormous potency. Its effect upon tissues is salubrious. Its application is simple, clean, non-irritating and not

involved in the tedious, expensive and complicated technique of other antiseptics. Its recent discovery makes its far reaching possibilities as yet unknown, and much of its amazing promise is still in the hands of the pioneers in its use.

"It is claimed that many Milwaukee firms are users of the product. There are also reprinted letters of recommendation from general managers, safety engineers, and even from a nurse and a physician of these commercial plants. These recommendations are of the unscientific and uncritical type common to such testimonials.

"To summarize; Gly-So-Iodonate is not the scientific masterpiece it is claimed to be; the statement of composition is obviously incorrect; the product is essentially semi-secret; its actions are virtually those of a solution of potassium mercuric iodid to which has been added a chemical hodgepodge; it is marketed under a nondescriptive and misleading name. In view of these facts, the Council has authorized publication of this report declaring Gly-So-Iodonate inadmissible to New and Nonofficial Remedies."

Details of Analysis

Alkaloids.—A few cubic centimeters of the original were evaporated to half-volume (removing alcohol), acidified with diluted sulphuric acid and tested with phosphotungstic acid. The test was negative. When a drop of 1-500 solution of quinin sulphate was added to 2 c.c. of G. S. I., a precipitate was formed immediately (due to the presence of alkali mercuric iodid). A 100 c.c. sample of G. S. I. was taken and the alcohol distilled over; the alcohol-free solution made ammoniacal was then shaken with three successive portions of chloroform. The combined chloroform extracts were then treated with water, made acid with diluted hydrochloric acid and the chloroform discarded. The aqueous acid extract was made ammoniacal, and extracted with three portions of chloroform, the chloroform solution was then filtered through cotton, the cotton washed with chloroform, and the chloroform evaporated in a tared beaker by means of a stream of *warm* air. The residue weighed 0.0001 gm.

Mercury.—(a) Fifty c.c. of G. S. I. were transferred to an Erlenmeyer flask, 10 c.c. of sodium hydroxid solution and 15 c.c. of solution of formaldehyde U. S. P. added. The flask was attached to a reflux condenser (to insure against loss of mercury) and the contents boiled for two hours. The precipitate was filtered off and washed well. A small volume of hot concentrated nitric acid, containing about 5 per cent. of hydrochloric acid, was poured in several portions on the filter (the filtrate being caught in the same Erlenmeyer flask as used for the reduction with formaldehyde solution). The solution was boiled for a few minutes, then cooled, made up to a volume of about 85 c.c. and transferred to a platinum dish; the washings brought the total volume up to 110 c.c. The mercury solution was electrolized with a current of 7 volts and 2-3 amperes. After one hour, the solution was removed by suction, and the dish washed with water, then with redistilled alcohol and then ether. After drying in a desiccator containing mercury and potassium hydroxid, the dish was weighed, heated to volatilize the mercury, and after cooling weighed again. The difference in weight was 0.0100 gm., equivalent to 0.020 per cent. of mercury. *(b)* A duplicate determination, carried out exactly as above, yielded 0.0155 gm., equivalent to 0.031 per cent. of mercury. *(c)* As a compensating check, 50 c.c. of the original were transferred to an Erlenmeyer flask, 25 c.c. of concentrated nitric acid added, and the contents of the flask boiled under a reflux for 1½ hours. The solution was electrolyzed as described under "*a*." The amount of mercury was 0.0142 gm., equivalent to 0.028 per cent. The average of the three determinations was 0.026 per cent. of mercury.

Platinum.—*(a)* A 100 c.c. sample of the original was transferred to an Erlenmeyer flask, formic acid added in excess of acidity, about ½ gm. of ammonium acetate added, and the contents boiled under a reflux condenser for 24 hours. The precipitated metal was filtered off, washed, dried, ignited and weighed in a tared porcelain crucible. The weight of the contents was 0.0125 gm., equivalent to 0.01 per cent. Examination of the contents showed a considerable amount of silica present. Hence, the per cent. of platinum is less than 0.01 per cent. *(*b*)* A 100 c.c. sample of the original was treated with sodium hydroxid solution and formaldehyde. The solution was boiled 4 hours under a reflux condenser; the precipitate, treated as described under "*a*," weighted 0.0121 gm. Silica was also present; hence, the platinum was less than 0.01 per cent.

Iodate and Iodide.—In order to be certain that the mercury was in the form of the complex alkali salt (K_2HgI_4 or Na_2HgI_2), it was necessary to determine the iodid (I^-). As iodate was also present, it was necessary to determine this also before the iodid could be calculated.

Iodate.—Twenty-five c.c. of the original were treated with an excess of diluted hydrochloric acid, 5 c.c. of potassium iodid solution added and titrated with tenth normal solution of sodium thiosulphate, starch being used as indicator. *(a)* 25 c.c. required 2.5 c.c. of the N/10 sodium thiosulphate solution, equivalent to 0.03 per cent. of sodium iodate. *(b)* 25 c.c. required 2.4 c.c. of the N/10 sodium thiosulphate solution, equivalent to 0.03 per cent. of sodium iodate.

Iodid.—Ten c.c. of the original were treated with a slight excess of diluted hydrochloric acid and 20 c.c. of approximately tenth normal solution of potassium iodate; the solution was boiled until free from iodin. After cooling, 10 c.c. of potassium iodid solution were added, and the excess of potassium iodate titrated with N/10 sodium thiosulphate solution. *(a)* The amount of sodium thiosulphate solution required was 17.55 c.c. Twenty c.c. of the potassium iodate solution were found by titration to be equivalent to 18.85 c.c. of N/10 sodium thiosulphate solution, and therefore equivalent to 18.85 c.c. of N/10 potassium iodate solution. From previous determinations, there had been found to be present iodate equivalent to 0.96 c.c. of N/10 potassium iodate solution; hence, the total amount of N/10 potassium iodate was 19.81 c.c. Subtracting 17.55 c.c. from 19.81 c.c. gives the amount of potassium iodate conusmed to oxidize all of the iodid to iodin. This is equivalent to 0.23 per cent. iodid (I^-). *(b)* Exact duplicate of "*a*." This shows, therefore, that there was 3.5 times as much iodid present as that theoretically necessary to convert the mercury compound to the ($HgI_4^=$) ion.

ADDENDA

The JOURNAL commented editorially on the foregoing report as follows:

"A" Formula or "The" Formula?

A quarter of a century ago, when the proprietary evil in the United States was at its worst, a common piece of advertising deceit was that of the fake formula. Knowing that reputable physicians will not prescribe secret remedies, some proprietary medicine concerns resorted to giving what purported to be a formula. On its face, the "formula" was impressive—at least to one not an expert in chemistry. Actually, such formulas were pure fabrications, chemically impossible. The real composition was seldom divulged by such feints at honesty. After the American Medical Association created its own chemical laboratory, the Association chemists demonstrated repeatedly the absurdity of the seriocomic chemistry of even some of the better grade of pharmaceutic manufacturers. It was not long before the crude chemistry and cruder dishonesty of pharmaceutic concerns began to disappear. Yet today there are still a few firms that endeavor to lend plausibility to their wares by resurrecting old methods. On another page [1] is a report of the Council on Pharmacy and Chemistry on Gly-So-Iodonate. The product is exploited to the profession as "the bactericide the medical world has searched for since the days of Lister." A "formula," both qualitative and quantitative, appears on the label. Chemically, the formula is absurd. As the report shows, some of the "declared ingredients" are obviously incompatible, while the chemical laboratory has found that other ingredients are not present in the amounts claimed. Physicians are being urged to use this unscientific mixture. The favorite method of approach, however, seems to be through industrial concerns; most of the inquiries regarding industrial concerns seeking advice in order to present it to the respective business managers. Large employers of labor who seek to protect their employees from infection hazards should be given the facts regarding the probable value of vaunted proprietary germicidal agents. From a standpoint both of economy and of rational procedure, it is evident that there are plenty of such agents which can be used to better advantage than this nostrum. Mercuric chlorid is still a favorite, and convenient size tablets are listed by all good pharmaceutic houses; and, should the coagulating action of mercuric chlorid be undesirable, there are on the market accepted brands of potassium mercuric iodid [2] (which may be considered the active ingredient in Gly-So-Iodonate though not declared); there are also the chlorin antiseptics,[3] and tried and true official tincture of iodin—and a host of others. Of course, the choice of an antiseptic depends on the condition for which it is to be used. Certain it is, however, there is no scientific basis for mixing antiseptics in any such hodgepodge manner as is exemplified by the irrational and mislabeled Gly-So-Iodonate.—*(Journal, A. M. A., Dec. 22, 1923, p. 2118).*

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[1] Gly-So-Iodonate: Report of the Council on Pharmacy and Chemistry, this issue, page 2132.

[2] The following brands are described in New and Nonofficial Remedies, 1923: Mercury and Potassium Iodide, Merck; Mercury and Potassium Iodid, P. W. R.; Kalmerid Germicidal Tablets Potassium Mercuric Iodide, Davis and Geck. Solutions can also be prepared extemporaneously: mercuric chlorid, 0.06 gm.; potassium iodid, 0.6 gm.; water to make 100 c.c.

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[3] Surgical Solution of Chlorinated Soda, N. N. R. (Dakin's Solution) may be prepared according to methods described in N. N. R., or one of the accepted proprietary sodium hypochlorite solutions may be empolyed. There are also a number of accepted brands of Chloramine-T and Dichloramine-T described in New and Nonofficial Remedies, 1923.

PART III

REPORTS NOT PREVIOUSLY PUBLISHED

NOTE ON A COMPOUND OF BENZOCAIN WITH IODIN

L. E. Warren, Ph.C., B.S.

Attention was called in a previous paper [1] to a compound of benzocain with iodin. This was described as occurring in beautiful, iridescent crystals which, in the absence of confirmatory tests, might be mistaken for the curious quinin compound, herapathite (quinin iodo-sulphate). Since this brief mention of the benzocain-iodin compound was published, some additional observations have been made which it was thought worth while to record.

For the tests herein described, 1 gm. of benzocain was placed in 100 c.c. of water and hydrochloric acid added, a few drops at a time with shaking, until all but a very few of the crystals had been dissolved. The mixture was then filtered and a portion of the filtrate subjected to the following test:

> To about 1 c.c. of the solution of benzocain (1: 100) in very dilute hydrochloric acid add about 1 c.c. of iodin solution, shake the mixture and allow to stand for 10 minutes with occasional agitation. A reddish-brown precipitate forms which changes to beautiful, scintillating scales having a bronze-like lustre. The crystals are best observed by agitating the test tube in direct sunlight.

To the naked eye the precipitate reminds the observer of herapathite. Under the low power of the microscope the crystals appear as irregular aggregations of tables and prisms, most of which are brown; but many are brilliant yellow or brass colored; some are grass green; others are blue or dark bluish violet and occasionally one is observed which exhibits prismatic colors. Combinations of two or more of these varieties are common. The writer has not observed any compound of the other local anesthetics with iodin which resembles this. In the great variety of color and beauty of its forms, it appears to be unique.

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[1] Warren, L. E.: J. Am. Pharm. A. **12**: 516, 1923.

The precipitate does not form in hot water and it was found to be too soluble in cold water for the reaction to be of value in the quantitative separation of benzocain from other organic substances. The compound melts in hot water to a brownish, black liquid. The precipitate is soluble in glycerin. Solutions containing much alcohol do not give the precipitate *(distinction from herapathite)*. This will be noted in greater detail later.

Although to the naked eye the crystals of the benzocain-iodin compound somewhat resemble iodo-quinin sulphate (herapathite), there are some differences discernible. The benzocain compound consists for the most part of larger particles than the herapathite precipitate and, if shaken in the precipitating liquid, the crystals do not show so much of the bronze-like lustre which is such a notable property of herapathite. Further, owing to the greater proportion of yellow particles in the benzocain compound, the scintillations are brighter than in herapathite.

Another distinguishing difference between the two compounds lies in the method of preparations. Herapathite may be prepared as follows:

> Dissolve 0.5 gm. of quinin sulphate in 10 c.c. of 50 per cent. alcohol, add 1 c.c. of dilute sulphuric acid and add tincture of iodin, drop by drop, with agitation so long as a precipitate continues to form.

Under the same conditions the benzocain-iodin compound does not form since the presence of much alcohol prevents precipitation. Under the low power of the microscope there are very noticeable distinctions between the crystals of the two compounds. Herapathite crystals are mostly pale green, thin rhombic plates. In the benzocain compound, the crystals are thicker than in herapathite; the brass-yellow forms are more numerous, the green ones are less noticeable and most of the benzocain-iodin compound crystals are brown.

A quantity of the benzocain-iodin compound was prepared, the crystalline precipitate collected on a filter, washed with cold water and dried in the air. The product was a greenish-black, coarsely, crystalline powder, having a bronze-like lustre. The air-dried crystals lost about 0.45 per cent. of their weight when dried over sulphuric acid for 48 hours. At 100 C., the compound suffers loss through decomposition.

A determination of the total iodin in the compound[2] indicated about 57.5 per cent. The theoretical percentage of iodin in a compound having the formula $C_6H_4.NH_2COOC_2H_5.HI+H_2O$ is 40.8 and the water of hydration content 5.8 per cent. The theoretical content for a compound without water of hydration is 43.3 per cent. A compound having the composition $C_6H_4.NH_2COOC_2H_5 2HI+H_2O$ contains 57.82 per cent. of iodin and 4.10 per cent. of water of hydration. It seems likely, therefore, that the benzocain-iodin compound contains two equivalents of iodin for each molecule of benzocain.

ESKOSAN AND ESKOSAN CUM METHYL SALICYLATE

Eskosan, sold by Esko Products Company of Phillipsburg, N. J., was presented to the Council. As a check upon the claims made, the laboratory examined the product. It is claimed to be composed of U. S. P. ingredients only. Among the ingredients claimed are pyrophyllite (a hydrated aluminum silicate) and terpineol. Neither of these substances is described in the U. S. Pharmacopeia. The other ingredients claimed to be present in Eskosan are 3 per cent. of resublimed iodin, 2 per cent. of phenol, 8 per cent. of acetanilid together with lanolin and petrolatum.

Eskosan Cum Methyl Salicylate is claimed to be Eskosan to which 5 per cent. of methyl salicylate has been added. Eskosan is described by the exploiter as "The Iodin Ointment." The action of iodin is stressed throughout the Eskosan circular.

It is well known that phenol combines with iodin in the presence of a catalyst, e. g., mercuric chlorid (Weselsky & Casiwetz, Ber. **2**:523, 1869). Since it is recognized that the effect of a catalyst is to increase the rate of reaction only, it seems probable that phenol and iodin in admixture would combine slowly at ordinary temperature in the absence of any catalyst. That the two substances do combine under such circumstances was shown by the Chemical Laboratory in the case of Iocamfen and Iocamfen Ointment (Rep. A. M. A. Chem. Lab. **9**:118, 1916). In view of this it was considered necessary to test the Eskosan Ointment and the Eskosan Cum Methyl Salicylate for free iodin. The method used was as follows:

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[2] Dissolve 0.2-0.3 gm. of material as completely as possible in 5 c.c. of 10 per cent. sodium hydroxid and 100 c.c. of warm water, add 35 c.c. of 7 per cent. potassium permanganate, cover with a watch glass and add 10 c.c. of nitric acid. Heat the mixture on a steam bath, keeping covered until spattering ceases, remove the cover and evaporate the mixture to dryness. Treat the residue with 5 c.c. of potassium permanganate solution and 5 c.c., of nitric acid and again evaporate the mixture to dryness. Dissolve the residue in 50 c.c. of water, add 5 c.c. of nitric acid and 40 c.c. of saturated sulphur dioxid solution—an excess of sulphur dioxid must be present and the solution must be clear. Add an excess of silver nitrate solution, boil until the sulphur dioxid is expelled and the silver iodid has flocculated. Collect the silver iodid, wash, dry and weigh in the usual way. (Modified from the method of Seeker and Mathewson, Bur. Chem. Circ., 65.)

A portion of the material was dissolved in chloroform so far as possible and the mixture passed through a dry filter. The chloroform layer was shaken with a very dilute solution of potassium iodid containing a trace of hydrochloric acid and the aqueous layer decanted through a wetted filter. A portion of the filtrate was mixed with starch paste. Another portion was shaken with chloroform.

The results from these tests were in each case negative. Therefore, it was concluded that free iodin is not present either in Eskosan or in Eskosan Cum Methyl Salicylate.

NOTE ON FRONTIER ASTHMA CO. TREATMENT

The preparations examined were in the form of liquid and tablets. The former was contained in an eight ounce bottle and purported to be a prescription. The label bore the statement that the preparation had been prescribed for a Mrs. Mary Kelly by a "Dr. Stanton." The label bore the prescription number 521,586 and the date of July 25, 1923. The other portions of the treatment consisted of tablets contained in two small envelopes without the name of the patient and without any prescription number.

A specimen of Frontier Asthma Co. Treatment (liquid) was examined in the A. M. A. Chemical Laboratory in 1916 (Reports Chem. Lab., A. M. A. **9**:114, 1916). At that time, apparently, there were no tablets in the treatment. The results of the analysis were approximately as follows:

Ammonium iodid	5.20 gm. per 100 c.c.
Potassium iodid	4.90 gm. per 100 c.c.
Sodium iodid	5.50 gm. per 100 c.c.
Caffein	2.30 gm. per 100 c.c.
Arsenic (as arsenous oxid)	0.05 gm. per 100 c.c.
Water and coloring to make	100.00 c.c.

Qualitative tests on the specimen (liquid) recently received demonstrated the presence of caffein, an iodid, an arsenic compound and salts of ammonia, potassium and sodium. Emodin bearing drugs, alkaloids (other than caffein), phenobarbital and bromids were absent. So far as qualitative tests are concerned the liquid portion of the treatment appears to have the same composition as that analyzed in 1916.

TABLETS

The tablets were received in two envelopes. The tablets were gray in color and had a faint, spicy odor somewhat like elm bark. Qualitative tests demonstrated the absence of alkaloids, ammonium salts, emodin-bearing drugs, heavy metals and glycyrrhiza. Starch and sucrose (cane sugar) were present. A ground vegetable drug was present which gave a very small amount of a greenish residue on extraction with ether. The residue had a faint spicy odor. The drug was not identified but it is evident that it is not very potent. The tablets in the two envelopes appeared to be identical.

NEO-SILVOL

Neo-Silvol is a colloidal silver iodid compound, manufactured by Parke, Davis & Co., Detroit, Mich. According to the definition, it is a compound of silver iodid with a soluble gelatin base containing 18 to 22 per cent. silver. The product was submitted to the Council on Pharmacy and Chemistry for inclusion in New and Nonofficial Remedies. The manufacturer stated that Neo-Silvol is prepared by heating freshly precipitated silver oxid with gelatin (which has been previously dissolved in dilute alkaline solution) until the silver oxid has been reduced to metallic silver in a colloidal state of subdivision. The solution is treated with iodin which combines with the silver. The liquid is then evaporated to dryness *in vacuo*.

As it seemed that the product might contain an excess of iodin over that required to unite in molecular proportion with the silver present, an examination was made.[1]

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[1] A solution resembling Neo-Silvol can be prepared by treating silvol with iodin-potassium iodid solution. It is interesting to note how the dark brown silvol solution turns to the light color on addition of iodin. In similar manner, protargin-mild acts when treated with chloramin-T.

Qualitative tests showed the presence of iodin. Quantitative estimations were also made:

Silver iodid found	19.87 per cent.
Equivalent to iodin	10.73 per cent.
Iodin, total (Carius)	13.50 per cent.

From the analysis it is evident that the product contained about 2.8 per cent. iodin in excess of that needed for combination with the silver. In view of this the manufacturer agreed to include the following in the statement of method of preparation: "The finished product contains 1 to *3 per cent. of combined iodin in excess* of that required for combination with silver."

Details of Analysis

Iodin.—The weighed sample was determined according to the method of Carius, using excess of silver nitrate (a) 0.4712 gm. of Neo-Silvol yielded 0.1183 gm. of silver iodid, equivalent to 13.55 per cent. of iodin; (b) 0.5499 gm. of the sample yielded 0.1366 gm. silver iodid, equivalent to 13.44 per cent. iodin.

Silver iodid.—Silver iodid was determined according to the method supplied by the manufacturer:

> Transfer about 1 Gm. of neo-silvol, accurately weighed, to an 8 ounce Erlenmeyer flask containing 100 Cc. water and heat on steam bath until "solution" is effected. Add 5 Cc. of hydrochloric acid and boil gently over a flame for ten or fifteen minutes; cool; when sufficiently cool to handle, filter through a tared Gooch crucible containing a fairly thick pad of asbestos. Wash thoroughly with water acidulated with hydrochloric acid (0.3 per cent. hydrochloric acid). Dry at 100 C. and weigh as silver iodid.

(a) 1.3043 gm. of Neo-Silvol yielded 0.2587 gm. or 19.82 per cent. of silver iodid. (b) 1.4765 gm. yielded 0.2946 gm or 19.93 per cent. of silver iodid. The average, 19.87 per cent., is equivalent to 10.73 per cent. iodin present as iodid (I^-).

INDEX TO VOLUME 16

The names of authors appear in capitals, under which will be found the titles of their signed articles. Under the names of the proprietors appear the respective products to which reference is made. The names of the products also occur in alphabetical sequence.

PAGE
Acacia, absence of in Beauty Clays ... 80
Acid, citric, absence of in Beauty Clays ... 80
Acid hydriodic, determination of in Allen's Goiter Treatment ... 58
Aconitin hydrochlorid, incompatibility of with mercurochrome-220 soluble ... 8
Adams Wonder Capsules ... 51
Alcohol, in Allen's Goiter Treatment ... 57
  determination of in Van Ess ... 73
  in Van Ess ... 71
Aldehyd, test for in Carbon Tetrachlorid ... 48
Alkaloids, determination of in Van Ess ... 73
Allen, C. J.
  alleged originator of Allen's Goiter Treatment ... 55
Allen Remedy Company ... 55
Allen's Goiter Treatment ... 55
Alum, absence of in Beauty Clays ... 80
Alypin, incompatibility of with mercurochrome-220 soluble ... 8
Ammonium iodid, determination of in Allen's Goiter Treatment ... 57
Apomorphin hydrochlorid, incompatibility of with mercurochrome-220 soluble ... 8
Atropin sulphate, incompatibility of with mercurochrome-220 soluble 8
Apothesin, incompatibility of with mercurochrome-220 soluble ... 8
Antiseptics, The Chlorin ... 40

Baker's Analyzed Chemicals
  brand of carbon tetrachlorid ... 49
BARBER, M. A.
  see DARLING and ... 45
Benzocain, incompatibility of with mercurochrome-220 soluble ... 8
Benzocain ... 8, 11, 16, 18, 20, 23, 25, 97
Benzocain iodid ... 97
Benzocain with Iodin, note on a compound of ... 97
Boncilla Beautifier ... 74, 78
Brucin hydrochlorid, incompatibility of with mercurochrome-220 soluble ... 8
Butyn ... 14, 16 and 21
Butyn, incompatibility of with mercurochrome-220 soluble ... 8

Calcium carbonate, determination of in Owl Enamel Toilet Cream .. 64
Camphor, absence of in Beauty Clays ... 80

PAGE

Carbon disulphid, determination of in carbon tetrachlorid........48, 51
Carbon tetrachlorid, Medicinal 50
Carbon tetrachlorid
  M. C. W.. 49
  Cenco 49
  P. W. R.. 49
  Baker's, Analyzed 49
Carbon tetrachlorid, standards for............................ 51
Carbon tetrachlorid, analyses of............................. 49
Central Scientific Co.
  brand of carbon tetrachlorid.............................. 49
Cephaelin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Cinchonidin sulphate, incompatibility of with mercurochrome-220 soluble 8
Cinchonin sulphate, incompatibility of with mercurochrome-220 soluble 8
Chloramine T, Dichloramine T, and Preparations, examination of American made, by Paul Nicholas Leech, Ph.D................ 27
Chloramine T, oxidizing action of............................ 29
Chloramine T and Preparations, purity of market supply........... 30
"Chloramines," stability of................................... 38
Chloramines, stability of..................................... 39
Cocain hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Codein sulphate, incompatibility of with mercurochrome-220 soluble. 8
Comparison of Chloramines and "Surgical Solution of Chlorinated Soda" 28
Complexion Clays 74

DARLING, S. T., BARBER, M. A., and HACKER, H. D.
  Chenopodium in Hookworm Disease.......................... 45
Diacetyl-morphin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Dichloramine T, Halazone and Preparations, examination of American-made Chloramine T, by Paul Nicholas Leech, Ph.D............ 27
Dichloramine T, purity of market supply of...................... 34
Domino Complexion Clay.. 77

El Zair 65
Emetin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
English Complexion Clay, see Terra-Derma-Lax.................... 74
Eskosan 99
Eskosan Cum Methyl Salicylate................................. 99
Ethyl hydrocuprein hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Ethyl morphin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Eucain-β 7
β-eucain lactate, incompatibility of with mercurochrome-220 soluble.. 8
Ferrous Iodid, in Allen's Goiter Treatment......................57, 58
Free chlorin, test for in carbon tetrachlorid...................48, 51

GASTINE, G. PAGE
detection of carbon disulphid.................................... 46
Gelsemin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Glycerin, determination in Domino Complexion Clay................ 84
determination of, in Owl Enamel Cream..................... 64
Gly-So-Iodonate............................87, 88, 89, 90, 91 and 92

HACKER, H. D.: see DARLING and HACKER................. 45
Halazone and Preparations, examination of American-made Chloramine T, Dichloramine T, by Paul Nicholas Leech, Ph.D........ 27
HALL, M. C.
Carbon Tetrachlorid in Hookworm Disease.................... 42
HAMPTON, see NICHOLLS and............................... 43
Herapathite 20, 97, 98
Holocaine, see Phenacaine...................................... 22
Homatropin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Hydrastin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Hydrogen peroxid, absence of in Beauty Clays.................... 80

Identification of some Local Anesthetics, The...................... 10
Incompatibility of mercurochrome-220 soluble with Local Anesthetics and Alkaloids, by L. E. Warren, Ph.C., B.S.................. 7

Kerosene in Van Ess.. 71

LAKE, C. G.
Studies with Carbon Tetrachlorid............................. 43
LAMBERT, S. M.
Carbon Tetrachlorid in Hookworm Disease.................... 43
LEACH, C. N.
Carbon Tetrachlorid in Hookworm Disease.................... 43
Lead in Owl Enamel Toilet Cream.............................62, 64
Lead, determination of in Owl Enamel Cream.................... 64
Lead carbonate, determination of in Owl Enamel Toilet Cream..... 64
LEECH, PAUL NICHOLAS
Examination of American-made Chloramine-T, Dichloramine-T, Halazone and Preparations............................... 27
LEHNER
Opinion of "Analyzed Chemicals"............................ 50
London Times
dispatch concerning hookworm.............................. 43

Magnesium Sulphate, absence of in Beauty Clay.................. 80
McVAIL, J. B.
Carbon Tetrachlorid in Hookworm Disease.................... 44
McGOWAN, M. J.
exploiter of Beauty Clays.................................... 76
M. C. W. brand of carbon tetrachlorid............................ 49
Mercurochrome-220 soluble, incompatibility of with alkaloids........ 7

PAGE

Mineralava 77
Money in Mud 74
Morphin sulphate, incompatibility of with mercurochrome-220 soluble. 8
Mud, Money in 74

Narcein hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Narcotin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Nature's Beauty Clay 77
Neo-Silvol 101
NICHOLLS, L., and HAMPTON, G. C.
  Carbon Tetrachlorid in Hookworm Disease 43
Nicotin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Note on a Compound of Benzocain with Iodin 97
Note on Frontier Asthma Co. Treatment 100

Orthoform 8, 11, 13, 17, 19, 22
Owl Enamel Toilet Cream 62
OWL DRUG COMPANY 62

Papaverin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
Peralga 58, 59
PESSOA, S. B., see SMILLIE and 45
Phenacain 8, 11, 13, 15, 17, 19 and 22
Phenacain, incompatibility of with mercurochrome-220 soluble 8
Physostigmin sulphate, incompatibility of with mercurochrome-220 soluble 8
Phenol, absence of in Beauty Clays 80
Pilocarpin nitrate, incompatibility of with mercurochrome-220 soluble 8
P. W. R., brand of carbon tetrachlorid 49
Procain 8, 11, 13, 17, 19 and 22
Procain, incompatibility of with mercurochrome-220 soluble 8
Propaesin 8, 11, 13, 17, 19, 22
Propaesin, incompatibility of with mercurochrome-220 soluble 8

Quayles' "Bob-White Habit Sinker's" 52
Quinidin sulphate, incompatibility of with mercurochrome-220 soluble 8
Quinin and urea hydrochlorid, incompatibility of with mercurochrome-220 soluble 8
  hydrochlorid, incompatibility of with mercurochrome-220 soluble. 8
  iodo-sulphate 97
  sulphate in Van Ess 71

RADCLIFFE, L. G.
  method for the determination of carbon disulphid 46
Ryerson's Forty Minute Beauty Clay 77

Salicylic Acid, determination of in Domino Complexion Clay 83
Sanguinarin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8

PAGE

Scopolamin hydrobromid, incompatibility of with mercurochrome-220 soluble 8

SCHULTZ, W. H.
  Chloroform as an anthelmintic.... 42

Slendaform 84, 85, 86

SMILLIE, W. G., and PESSOA, S. B.
  Carbon Tetrachlorid in Hookworm Disease.... 45

Sodium borate, absence of Beauty Clays.... 82

Sodium salicylate, determination in Domino Complexion Clay.... 83

Solanin hydrochlorid, incompatibility of with mercurochrome-220 soluble 8

Starch paste, absence of in beauty clays.... 82

STOLZ, DR. CHARLES L.
  Caution in the use of Mercurochrome-220 soluble.... 7

Stovain, incompatibility of with mercurochrome-220 soluble.... 8

Strychnin sulphate, incompatibility of with mercurochrome-220 soluble 8

"Surgical Solution of Chlorinated Soda," Comparison of Chloramines 28

Syrup, ferrous iodid, presence of in Allen's Goiter Treatment.... 57

Talc (insoluble matter) estimation of in Owl Enamel Toilet Cream.. 63

Terra-Derma-Lax, "the English Complexion Clay".... 74

Thebain hydrochlorid, incompatibility of with mercurochrome-220 soluble 8

Tragacanth jelly, absence of in beauty clays.... 80

Tropacocain hydrochlorid....8, 11, 13, 15, 17, 19, 23, 24, 25, 26

Tropacocain hydrochlorid, incompatibility of with mercurochrome-220 soluble 8

Van Ess 70

Van Ess Laboratories.... 70

VELEY, V. H.
  analysis of carbon tetrachlorid.... 47

WALLER, A. D., analysis of a "hair wash".... 46

WARREN, L. E.
  Incompatibility of Mercurochrome-220 Soluble with Local Anesthetics and Alkaloids.
  The identification of Some Local Anesthetics....7, 10
  The Chemical Examination of Some Commercial Brands of Carbon Tetrachlorid
  Note on a Compound of Benzocain with Iodin....42, 97

WEISS, J. M.
  method for the determination of carbon disulphid.... 48

WILLCOX, W. H.
  examination of a shampoo.... 47

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